STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 125485

TO: Ralph J Gitomer
Location: 3e65 / 3e71
Wednesday, June 23, 2004
Art Unit: 1651
Phone: 272-0916
Serial Number: 10 / 648485

From: Jan Delaval
Location: Biotech-Chem Library
Rem 1A51
Phone: 272-2504

jan.delaval@uspto.gov

Search Notes

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=> fil reg
FILE 'REGISTRY' ENTERED AT 18:19:43 ON 23 JUN 2004
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   22 JUN 2004  HIGHEST RN 697737-72-7
DICTIONARY FILE UPDATES:  22 JUN 2004  HIGHEST RN 697737-72-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d his

     (FILE 'HOME' ENTERED AT 17:52:36 ON 23 JUN 2004)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 17:55:43 ON 23 JUN 2004
L1           570 S MATRIX(L)?METALLO?/CNS
L2           476 S ?METALLOPROTEASE?/CNS
L3          1457 S ?METALLOPROTEINASE?/CNS
L4          1940 S L1-L3

     FILE 'HCAPLUS' ENTERED AT 17:56:34 ON 23 JUN 2004
L5         15488 S MMP? OR MATRIXMETALLOPROTEASE OR MATRIXMETALLOPROTEINASE OR M
L6         32260 S L4
L7         19379 S ?METALLOPROTEASE? OR ?METALLOPROTEINASE?
L8         37648 S L5-L7
L9          1281 S L8 AND BASEMENT(L)MEMBRANE
L10          185 S L9 AND (SKIN OR EPIDERM? OR DERM?)
                 E BASEMENT MEMBRANE/CT
L11         5139 S E3-E6
L12         5139 S E3+OLD,NT,PFT
                 E E3+ALL
                 E E7+ALL
L13        16556 S E3+NT
L14          647 S L8 AND L11-L13
L15         1465 S L9,L14
                 E SKIN/CT
L16        97199 S E3+OLD,NT,PFT
                 E E3+ALL
L17        97192 S E7,E6+NT
L18          850 S E32+OLD,NT,PFT
L19        10495 S E34+OLD,NT,PFT
L20         6432 S E35+OLD,NT,PFT
L21        68544 S E38+OLD,NT,PFT
                 E SKIN DISEASE/CT
                 E E4+ALL
                 E E2+ALL
L22        68543 S E6,E7,E5+NT
L23          678 S E179+OLD,NT,PFT
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                E E181+ALL
L24          8037 S E3+NT
L25          2906 S E17+OLD,NT,PFT
                E E17+ALL
L26          4203 S E7+OLD,NT,PFT
L27          8526 S E8+OLD,NT,PFT
                E E6+ALL
L28          8037 S E3+NT
                E E14+ALL
L29         65858 S E2,E3,E1+NT
L30           183 S L15 AND L16-L29
L31           262 S L10,L30
                E WO2001-JP2507/AP,PRN
L32             1 S E3,E4
                E US2001-979712/AP,PRN
L33             1 S E3,E4
                E JP200-87574/AP,PRN
                E JP2000-87574/AP,PRN
L34             1 S E3,E4
L35             1 S L31 AND L32-L34
L36           194 S L31 AND (PD<=20010327 OR PRD<=20010327 OR AD<=20010327)
                E AMANO S/AU
L37           137 S E3,E18
                E MATSUNAGA Y/AU
L38            95 S E3
                E MATSUNAGA YUK/AU
L39             5 S E6
                E MATSUNAGA YU/AU
                E INOMATA S/AU
L40           101 S E3,E22
                E SHISEIDO/PA,CS
L41          5171 S E3,E4
L42            10 S L31 AND L37-L41
L43             1 S L35 AND L42
L44             1 S L35,L43
L45             9 S L42 NOT L44
L46            39 S L6 (L) INHIBIT? AND L36
                SEL DN AN 1 6 11 15 16 17 18 19 20 35 37
L47            11 S L46 AND E1-E33
                SEL DN AN 4 11
L48             9 S L47 NOT E34-E39
L49             9 S L44,L48
L50             5 S L49 NOT BASEMENT
L51           163 S L36 AND BASEMENT
L52             2 S L51 AND ARTIFICIAL(L)SKIN
L53             4 S L36 AND ARTIFICIAL(L)SKIN
L54             8 S L36 AND ARTIFICIAL?
L55             4 S L49 NOT L50
L56            11 S L52-L55
                SEL DN AN 5 6
L57             9 S L56 NOT E40-E45
L58             4 S L49 NOT L57
L59            22 S L57,L58,L45 AND L5-L58
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 18:19:06 ON 23 JUN 2004
L60            16 S E46-E61
L61            16 S L60 AND L4

     FILE 'REGISTRY' ENTERED AT 18:19:43 ON 23 JUN 2004

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L61 ANSWER 1 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **186207-03-4** REGISTRY
CN Proteinase inhibitor, TIMP 4 (9CI) (CA INDEX NAME)
OTHER NAMES:
CN TIMP-4
CN **Tissue inhibitor of metalloproteinase-4**
MF Unspecified
CI MAN
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, EMBASE, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
160 REFERENCES IN FILE CA (1907 TO DATE)
160 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:429032

REFERENCE 2: 140:402180

REFERENCE 3: 140:386673

REFERENCE 4: 140:333599

REFERENCE 5: 140:315978

REFERENCE 6: 140:300861

REFERENCE 7: 140:281832

REFERENCE 8: 140:144405

REFERENCE 9: 140:143714

REFERENCE 10: 140:75207

L61 ANSWER 2 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **161384-17-4** REGISTRY
CN **Proteinase, matrix metallo-, MT-MMP-1 (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN **Matrix metalloprotease 14**
CN **Matrix metalloproteinase 14**
CN **Matrix metalloproteinase MT 1**
CN **Matrix metalloproteinase MT-MMP-1**
CN **Matrix metalloproteinase MT1-MMP**
CN **Membrane type 1 matrix metalloproteinase**
CN **Membrane type-1 matrix metalloprotease**
CN **Membrane-type matrix metalloprotease 1**
CN **Membrane-type matrix metalloproteinase 1**
CN **Membrane-type matrix metalloproteinase MT1-MMP**
CN **Membrane-type metalloproteinase MT1-MMP**
CN MMP-14
CN MT-MMP1
CN MT1-MMP
MF Unspecified
CI MAN
SR CA

LC STN Files: AGRICOLA, BIOSIS, CA, CAPLUS, CIN, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PROC (Process); PRP (Properties)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
955 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
962 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:421960

REFERENCE 2: 140:421642

REFERENCE 3: 140:421550

REFERENCE 4: 140:421129

REFERENCE 5: 140:419865

REFERENCE 6: 140:419761

REFERENCE 7: 140:419742

REFERENCE 8: 140:418156

REFERENCE 9: 140:417926

REFERENCE 10: 140:404659

L61 ANSWER 3 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **152787-66-1** REGISTRY
CN Gelatinase B, pro- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Pro-MMP-9
CN Progelatinase B
CN **Promatrix metalloproteinase-9**
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, BIOSIS, CA, CAPLUS, CHEMCATS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
306 REFERENCES IN FILE CA (1907 TO DATE)
11 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
308 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:421864

REFERENCE 2: 140:404571

REFERENCE 3: 140:400355

REFERENCE 4: 140:389367

REFERENCE 5: 140:373027

REFERENCE 6: 140:336870

REFERENCE 7: 140:318946

REFERENCE 8: 140:301389

REFERENCE 9: 140:285325

REFERENCE 10: 140:281622

L61 ANSWER 4 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **148969-98-6** REGISTRY
CN Gelatinase A, pro- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 72-kDa type IV procollagenase
CN **Pro-matrix metalloproteinase-2**
CN Pro-MMP-2
CN Progelatinase A
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, BIOSIS, CA, CAPLUS, CHEMCATS, CIN, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); PROC (Process); PRP (Properties); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
503 REFERENCES IN FILE CA (1907 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
506 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:421129

REFERENCE 2: 140:404571

REFERENCE 3: 140:400355

REFERENCE 4: 140:389458

REFERENCE 5: 140:389367

REFERENCE 6: 140:389365

REFERENCE 7: 140:373027

REFERENCE 8: 140:372965

REFERENCE 9: 140:372611

REFERENCE 10: 140:372600

L61 ANSWER 5 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **146480-36-6** REGISTRY
CN Gelatinase B (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 92,000-Mol.-wt. gelatinase
CN 92,000-Mol.-wt. type IV collagenase
CN 92-kD Gelatinase
CN 92-kDa Gelatinase
CN 92-kDa Type IV collagenase
CN 95 kDa Type IV collagenase/gelatinase
CN Collagenase IV
CN Collagenase type IV
CN E.C. 3.4.24.35
CN Gelatinase MMP 9
CN **Matrix metalloprotease 9**
CN **Matrix metalloproteinase 9**
CN MMP 9
CN **Type IV collagen metalloproteinase**
CN Type IV collagenase
CN Type IV collagenase/gelatinase
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CEN, CHEMCATS, CIN, EMBASE, PROMT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PRP (Properties)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
4235 REFERENCES IN FILE CA (1907 TO DATE)
14 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4262 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:422318

REFERENCE 2: 140:422259

REFERENCE 3: 140:422070

REFERENCE 4: 140:421960

REFERENCE 5: 140:421864

REFERENCE 6: 140:421544

REFERENCE 7: 140:421526

REFERENCE 8: 140:421462

REFERENCE 9: 140:420372

REFERENCE 10: 140:419742

L61 ANSWER 6 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **146480-35-5** REGISTRY
CN Gelatinase A (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 72 kDa Gelatinase
CN 72 kDa Gelatinase type A
CN 72,000-Mol.-wt. gelatinase
CN 72,000-Mol.-wt. type IV collagenase
CN Collagenase IV
CN Collagenase type IV
CN E.C. 3.4.24.24
CN **Matrix metalloprotease 2**
CN **Matrix metalloproteinase 2**
CN MMP 2
CN **Type IV collagen metalloproteinase**
CN Type IV collagenase
CN Type IV collagenase/gelatinase
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CEN, CHEMCATS, CIN, EMBASE, PROMT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); OCCU (Occurrence); PROC (Process); PRP (Properties)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
4351 REFERENCES IN FILE CA (1907 TO DATE)
12 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4383 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:422318

REFERENCE 2: 140:422149

REFERENCE 3: 140:422070

REFERENCE 4: 140:421960

REFERENCE 5: 140:421642

REFERENCE 6: 140:421565

REFERENCE 7: 140:421526

REFERENCE 8: 140:421473

REFERENCE 9: 140:421174

REFERENCE 10: 140:421129

L61 ANSWER 7 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **145809-21-8** REGISTRY
CN Proteinase inhibitor, TIMP 3 (9CI) (CA INDEX NAME)
OTHER NAMES:
CN TIMP 3
CN **Tissue inhibitor of metalloproteinase-3**
MF Unspecified
CI MAN
SR CA
LC STN Files: AGRICOLA, BIOSIS, BIOTECHNO, CA, CAPLUS, CIN, EMBASE, PROMT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
550 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
553 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:429032

REFERENCE 2: 140:421174

REFERENCE 3: 140:417409

REFERENCE 4: 140:404972

REFERENCE 5: 140:404485

REFERENCE 6: 140:402180

REFERENCE 7: 140:400355

REFERENCE 8: 140:389191

REFERENCE 9: 140:369258

REFERENCE 10: 140:350803

L61 ANSWER 8 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **141907-41-7** REGISTRY
CN **Proteinase, matrix metallo- (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN **Matrix metalloendoproteinase**
CN **Matrix metalloprotease**
CN **Matrix metalloprotease HIPHUM35**
CN **Matrix metalloproteinase**
CN **Matrix-degrading metalloproteinase**
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CEN, CHEMCATS, CIN, PROMT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PROC (Process); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2929 REFERENCES IN FILE CA (1907 TO DATE)
16 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2949 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:429031

REFERENCE 2: 140:423687

REFERENCE 3: 140:421405

REFERENCE 4: 140:421397

REFERENCE 5: 140:419732

REFERENCE 6: 140:418294

REFERENCE 7: 140:416970

REFERENCE 8: 140:406814

REFERENCE 9: 140:406747

REFERENCE 10: 140:406737

L61 ANSWER 9 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **140208-24-8** REGISTRY
CN Proteinase inhibitor, TIMP 1 (9CI) (CA INDEX NAME)
OTHER NAMES:
CN EPA proteins
CN Erythroid-potentiating activity proteins
CN Fibroblast collagenase inhibitor
CN Gene TIMP1 proteins
CN **Metalloproteinase inhibitor 1**

CN Protein EPA
CN Protein TIMP
CN Protein TIMP-1
CN TIMP
CN TIMP 1
CN TIMP-1
CN TIMP-1 proteins
CN **Tissue inhibitor of metalloproteinase-1**
CN **Tissue inhibitor of metalloproteinase-1**
MF Unspecified
CI MAN
SR CA
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CIN, EMBASE, PROMT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2194 REFERENCES IN FILE CA (1907 TO DATE)
39 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2204 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:429032

REFERENCE 2: 140:422292

REFERENCE 3: 140:422070

REFERENCE 4: 140:421960

REFERENCE 5: 140:421526

REFERENCE 6: 140:421174

REFERENCE 7: 140:420372

REFERENCE 8: 140:419967

REFERENCE 9: 140:418499

REFERENCE 10: 140:418207

L61 ANSWER 10 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **124861-55-8** REGISTRY
CN Proteinase inhibitor, TIMP 2 (9CI) (CA INDEX NAME)
OTHER NAMES:
CN TIMP 2
CN TIMP-2 proteinase inhibitor
CN **Tissue inhibitor metalloproteinase-2**
DR 127497-59-0
MF Unspecified

CI MAN
SR CA
LC STN Files: ADISINSIGHT, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CIN, DDFU, DRUGU, EMBASE, MEDLINE, PHAR, PROMT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1554 REFERENCES IN FILE CA (1907 TO DATE)
34 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1558 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:429032

REFERENCE 2: 140:421526

REFERENCE 3: 140:421174

REFERENCE 4: 140:421129

REFERENCE 5: 140:418528

REFERENCE 6: 140:418156

REFERENCE 7: 140:412218

REFERENCE 8: 140:404972

REFERENCE 9: 140:404718

REFERENCE 10: 140:404659

L61 ANSWER 11 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **86102-31-0** REGISTRY
CN Proteinase inhibitor, TIMP (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Metalloproteinase elastase inhibitor**
CN TIMP
CN **TIMP metalloproteinase inhibitor**
CN TIMP proteinase inhibitor
CN **Tissue inhibitor of matrix metalloproteinase**
CN **Tissue inhibitor of metalloproteinase**
MF Unspecified
CI MAN
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAPLUS, CIN, PHAR, PROMT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
716 REFERENCES IN FILE CA (1907 TO DATE)
22 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
720 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:405091

REFERENCE 2: 140:404291

REFERENCE 3: 140:402121

REFERENCE 4: 140:389274

REFERENCE 5: 140:372735

REFERENCE 6: 140:354463

REFERENCE 7: 140:354461

REFERENCE 8: 140:350299

REFERENCE 9: 140:336696

REFERENCE 10: 140:333599

L61 ANSWER 12 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **79955-99-0** REGISTRY
CN Stromelysin 1 (9CI) (CA INDEX NAME)
OTHER NAMES:
CN E.C. 3.4.24.17
CN **Matrix metalloprotease 3**
CN **Matrix metalloproteinase 3**
CN **Matrix metalloproteinase MMP-3**
CN MMP-3
CN Neutral proteoglycanase
CN Proteoglycanase
CN Stromelysin
CN Transin
DR 107087-03-6, 118368-07-3
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CEN, CHEMCATS, CIN, EMBASE, IPA, PROMT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological

study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2483 REFERENCES IN FILE CA (1907 TO DATE)
28 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2493 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:423689

REFERENCE 2: 140:423477

REFERENCE 3: 140:422310

REFERENCE 4: 140:422305

REFERENCE 5: 140:421960

REFERENCE 6: 140:421764

REFERENCE 7: 140:421726

REFERENCE 8: 140:421655

REFERENCE 9: 140:421628

REFERENCE 10: 140:420372

L61 ANSWER 13 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **68651-95-6** REGISTRY
CN Proteinase, procollagen C-terminal (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **BMP-1 metalloproteinase**
CN Carboxylprocollagen peptidase
CN Peptidase, procollagen C-terminal
CN Procollagen C-proteinase
CN Procollagen C-terminal proteinase
CN Procollagen carboxypeptidase
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, BIOSIS, CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
86 REFERENCES IN FILE CA (1907 TO DATE)
86 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:266326

REFERENCE 2: 140:71032

REFERENCE 3: 140:15057

REFERENCE 4: 139:375014

REFERENCE 5: 139:317470

REFERENCE 6: 139:303564

REFERENCE 7: 139:245665

REFERENCE 8: 139:223711

REFERENCE 9: 139:192518

REFERENCE 10: 139:175703

L61 ANSWER 14 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **9040-48-6** REGISTRY
CN Gelatinase (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Collagenase IV
CN Collagenase type IV
CN **Type IV collagen metalloproteinase**
CN Type IV collagenase
CN Type IV collagenase/gelatinase
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS, CIN, CSCHEM, EMBASE, PIRA, PROMT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1143 REFERENCES IN FILE CA (1907 TO DATE)
11 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1146 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:420764

REFERENCE 2: 140:388204

REFERENCE 3: 140:350580

REFERENCE 4: 140:350579

REFERENCE 5: 140:333599

REFERENCE 6: 140:309376

REFERENCE 7: 140:309375

REFERENCE 8: 140:301335

REFERENCE 9: 140:297494

REFERENCE 10: 140:283257

L61 ANSWER 15 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **9004-06-2** REGISTRY
CN Elastase (9CI) (CA INDEX NAME)
OTHER NAMES:
CN E.C. 3.4.21.11
CN E.C. 3.4.21.36
CN E.C. 3.4.21.37
CN E.C. 3.4.24.65
CN E.C. 3.4.4.7
CN Elaszym
CN Macrophage metalloelastase
CN **Matrix metalloprotease 12**
CN **Matrix metalloproteinase-12**
CN Medullasin
CN **Metalloproteinase HME**
CN MMP 12
CN Neutrophil Elastase
CN Pancreatopeptidase E
CN Peptidase, pancreato-, E
CN Proteinase, bone marrow serine
DR 9001-21-2, 139074-64-9, 75603-19-9, 83682-98-8
MF Unspecified
CI COM, MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, NAPRALERT, NIOSHTIC, PHAR, PIRA, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
8287 REFERENCES IN FILE CA (1907 TO DATE)
268 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
8298 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:422456

REFERENCE 2: 140:422406

REFERENCE 3: 140:421655

REFERENCE 4: 140:421377

REFERENCE 5: 140:420382

REFERENCE 6: 140:419882

REFERENCE 7: 140:417137

REFERENCE 8: 140:412336

REFERENCE 9: 140:406821

REFERENCE 10: 140:406747

L61 ANSWER 16 OF 16 REGISTRY COPYRIGHT 2004 ACS on STN
RN **9001-12-1** REGISTRY
CN Collagenase (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Aspergillopeptidase C
CN Azocollase
CN Brachyurin
CN Clostridiopeptidase A
CN Clostridiopeptidase I
CN Clostridiopeptidase II
CN Clostridium histolyticum collagenase
CN Collagen peptidase
CN Collagen protease
CN Collagenase A
CN Collagenase MMP-1
CN E.C. 3.4.24.3
CN E.C. 3.4.24.34
CN E.C. 3.4.24.7
CN E.C. 3.4.4.19
CN E.C. 3.4.99.5
CN Euphaulysin
CN Interstitial collagenase
CN Iruxol
CN Kollaza
CN Liberase
CN Liberase Blendzyme IV
CN **Matrix metalloprotease MMP-ABT**
CN **Matrix metalloprotease-1**
CN **Matrix metalloproteinase-1**
CN **Matrix metalloproteinase-18**
CN **Matrix metalloproteinase-8**
CN Metallocollagenase
CN **Metalloproteinase-1**
CN MMP-1
CN MMP-8
CN Morikraz
CN Nucleolysin
CN Peptidase, clostridio-, A
CN Proteinase, Clostridium histolyticum, A
CN Santyl
CN Soycollagestin
DR 37288-86-1, 39433-96-0
MF Unspecified
CI COM, MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,

MRCK*, MSDS-OHS, PHAR, PIRA, PROMT, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
8304 REFERENCES IN FILE CA (1907 TO DATE)
73 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
8325 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:423689

REFERENCE 2: 140:423477

REFERENCE 3: 140:422481

REFERENCE 4: 140:422305

REFERENCE 5: 140:421960

REFERENCE 6: 140:421726

REFERENCE 7: 140:421655

REFERENCE 8: 140:421628

REFERENCE 9: 140:421271

REFERENCE 10: 140:421174

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FILE COVERS 1907 - 23 Jun 2004 VOL 140 ISS 26
FILE LAST UPDATED: 22 Jun 2004 (20040622/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot l59

L59 ANSWER 1 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:706920 HCAPLUS
DN 139:218977
ED Entered STN: 10 Sep 2003
TI **Matrix metalloproteinase** inhibitors containing catechins, procyanidins, and/or mangostins
IN Yokokawa, Yoshihiro; **Inomata, Shinji**
PA **Shiseido** Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61K007-48
ICS A61K007-00
CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2003252745	A2	20030910	JP 2002-52878	20020228
PRAI JP 2002-52878		20020228		

AB The invention relates to **matrix metalloproteinase** (**MMP**) inhibitors suitable for use in **skin** antiaging cosmetic compns., wherein the **MMP** inhibitors contain catechins, procyanidins, and/or mangostins. The inhibitory effect of α-mangostin, procyanidin B-2, and epicatechin on **MMP**-9, **MMP**-3, and **MMP** 1 activities were in vitro tested. Also, a cream containing γ-mangostin 0.01 and other ingredients q.s. to 100 % was formulated.
ST catechin procyanidin mangostin **matrix metalloproteinase** inhibitor cosmetic
IT **Cosmetics**
(antiaging; **matrix metalloproteinase** inhibitors containing catechins, procyanidins, and/or mangostins)
IT **Cosmetics**
(creams; **matrix metalloproteinase** inhibitors containing catechins, procyanidins, and/or mangostins)
IT **Basement membrane**
(degradation inhibitors; **matrix metalloproteinase** inhibitors containing catechins, procyanidins, and/or mangostins)
IT Collagens, biological studies
Elastins
Laminins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(degradation inhibitors; **matrix metalloproteinase** inhibitors containing catechins, procyanidins, and/or mangostins)
IT **Cosmetics**
(emulsions; **matrix metalloproteinase** inhibitors containing catechins, procyanidins, and/or mangostins)
IT **Cosmetics**
(foundations; **matrix metalloproteinase** inhibitors containing catechins, procyanidins, and/or mangostins)

IT **Cosmetics**
(gels; **matrix metalloproteinase** inhibitors containing catechins, procyanidins, and/or mangostins)
IT **Cosmetics**
(lotions; **matrix metalloproteinase** inhibitors containing catechins, procyanidins, and/or mangostins)
IT Human
(**matrix metalloproteinase** inhibitors containing catechins, procyanidins, and/or mangostins)
IT Procyanidins
Tannins
RL: COS (Cosmetic use); PAC (Pharmacological activity); BIOL (Biological study); USES (Uses)
(**matrix metalloproteinase** inhibitors containing catechins, procyanidins, and/or mangostins)
IT **141907-41-7, Matrix metalloproteinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **matrix metalloproteinase** inhibitors containing catechins, procyanidins, and/or mangostins)
IT **9001-12-1, Matrix metalloproteinase-1**
9040-48-6, Gelatinase **79955-99-0, Matrix metalloproteinase-3 146480-36-6, Matrix metalloproteinase-9**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**matrix metalloproteinase** inhibitors containing catechins, procyanidins, and/or mangostins)
IT 490-46-0, (-)-Epicatechin 6147-11-1, α-Mangostin 12798-56-0, Procyanidin A-1 20315-25-7, Procyanidin B-1 20931-37-7, β-Mangostin 23567-23-9, Procyanidin B-3 29106-49-8, Procyanidin B-2 29106-51-2, Procyanidin B-4 31271-07-5, γ-Mangostin 37064-30-5, Procyanidin C-1 41743-41-3, Procyanidin A-2 110343-03-8, Procyanidin C-3
RL: COS (Cosmetic use); PAC (Pharmacological activity); BIOL (Biological study); USES (Uses)
(**matrix metalloproteinase** inhibitors containing catechins, procyanidins, and/or mangostins)

L59 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:550188 HCAPLUS
ED Entered STN: 18 Jul 2003
TI active inhibitor and make-up charge for anti- aging [Machine Translation].
IN **Inomata, Shinji**; Umishio, Kenichi; Kobayashi, Koji; Hineno, Teruhiko
PA **Shiseido** Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61K007-48
ICS A61K007-00; A61K035-78; A61P003-00; A61P017-00; A61P043-00
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2003201229	A2	20030718	JP 2002-207951	20020717
PRAI JP 2001-325605	A	20011023		

AB [Machine Translation of Descriptors]. It possesses the competition action which is superior vis-a-vis the activity of (**MMPs**) which produces big effect on aging of the **skin** preventing the disassembly of the **skin** extracellular matrix component (for example elastin and , proteoglycan, **basement membrane** component and collagen etc.) which is related to aging of the **skin** deeply, prevention **skin** aging improve the **MMPs** active inhibitor which & can preventing, it offers the make-up charge for anti-

aging. Coconut (Cocos nucifera), (Blumea balsamifera), (Illicium verum) and brasiliensis (Juniperus Brasiliensis), alb (Salix alba), guarana (Paullinia cupana), being attached (Smila X) the **MMPs** active inhibitor, and the make-up charge for anti- aging which contain or more which is chosen from midst of 3 kinds (S. officinalis, S.aristolochiaefolia and S.aspera) the plant or that solvent extract of 1 kind or 2 kinds.

L59 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:550178 HCAPLUS
DN 139:106122
ED Entered STN: 18 Jul 2003
TI **Matrix metalloproteinase** inhibitors containing plants (extracts)
IN **Inomata, Shinji**; Umishio, Kenichi; Kobayashi, Koji; Ota, Masahiro
PA **Shiseido** Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61K007-00
ICS A61K035-78; A61P043-00
CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 7
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2003201214	A2	20030718	JP 2002-207952	20020717
PRAI JP 2001-325606	A	20011023		

AB **Matrix metalloproteinase** inhibitors, useful for preventing or treating **skin** aging, contain ≥1 plant selected from Woodfordia floribunda, avocado (Persea americana), Rheum, Cassia angustifolia, mangosteen, tamarind, Bergenia ciliata, Luehea divaricata, L. grandiflora, L. ochrophylla, L. paniculata, L. rufescens, Arctium lappa, Arctium minus, Anemopaegma arvense, Anemopaegma glaucum, Erythroxylum vaccinifolium, Margaritaria nobilis, and Pouteria obtusifolia or their exts. A MeOH extract of P. americana bark inhibited human **MMP**-1, -3, and -9. A solid foundation containing an EtOh extract of P. americana was also formulated.
ST **MMP** inhibitor avocado ext antiaging cosmetic; **matrix metalloproteinase** inhibitor plant ext antiaging cosmetic
IT **Cosmetics**
(antiaging; **matrix metalloproteinase** inhibitors containing Woodfordia floribunda, avocado and Rheum, or their exts. for antiaging cosmetics)
IT **Basement membrane**
(degradation inhibitors; **matrix metalloproteinase** inhibitors containing Woodfordia floribunda, avocado and Rheum, or their exts. for antiaging cosmetics)
IT Collagens, biological studies
Elastins
Laminins
Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(degradation inhibitors; **matrix metalloproteinase** inhibitors containing Woodfordia floribunda, avocado and Rheum, or their exts. for antiaging cosmetics)
IT Anemopaegma arvense
Anemopaegma glaucum
Arctium lappa
Arctium minus
Bergenia ciliata

Erythroxylum vaccinifolium
Garcinia mangostana
Luehea divaricata
Luehea grandiflora
Luehea ochrophylla
Luehea paniculata
Luehea rufescens
Margaritaria nobilis
Persea americana
Pouteria obtusifolia
Rhubarb (Rheum)
Senna (Cassia angustifolia)
Tamarind (Tamarindus indica)
Woodfordia floribunda
(**matrix metalloproteinase** inhibitors containing Woodfordia floribunda, avocado and Rheum, or their exts. for antiaging cosmetics)

IT Human
(**matrix metalloproteinases** of; **matrix metalloproteinase** inhibitors containing Woodfordia floribunda, avocado and Rheum, or their exts. for antiaging cosmetics)

IT **9001-12-1**, Collagenase **9040-48-6**, Gelatinase **79955-99-0**, Stromelysin **141907-41-7**, **Matrix metalloproteinase 146480-36-6**, **Matrix metalloproteinase** 9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**matrix metalloproteinase** inhibitors containing Woodfordia floribunda, avocado and Rheum, or their exts. for antiaging cosmetics)

L59 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:550177 HCAPLUS
DN 139:106121
ED Entered STN: 18 Jul 2003
TI **MMP** inhibitors and **skin** preparations containing plant (extracts)
IN **Inomata, Shinji**; Umishio, Kenichi; Kobayashi, Koji; Satake, Motoyoshi; Sekita, Setsuko; Takano, Akito
PA **Shiseido** Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61K007-00
ICS A61K007-48; A61K035-78; A61P017-16; A61P043-00
CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 7
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2003201212	A2	20030718	JP 2002-263190	20020909
PRAI	JP 2001-325607	A	20011023		

AB **MMP** inhibitors contain ≥1 plant selected from Schima noronhae, Loranthus, Cinnamomum iners, Desmodium triquetrum, Artocarpus elasticus, Equisetum debile, and Bombax ceiba or their exts. Also claimed are **skin** prepns. containing the plant or the exts. to prevent or treat **skin** aging. A MeOH extract of leaves and twigs of D. triquetrum inhibited human **MMPs**-1, -3, and -9. An emulsion containing EtOAc extract of D. triquetrum was also formulated.
ST **matrix metalloprotease** inhibitor plant ext antiaging cosmetic; Desmodium ext **MMP** inhibitor **skin** prepn aging prevention
IT **Cosmetics**

(antiaging; **skin** prepns. containing plant (exts.) as **matrix metalloprotease** inhibitors)
IT **Basement membrane**
(degradation inhibitors; **skin** prepns. containing plant (exts.) as **matrix metalloprotease** inhibitors)
IT Collagens, biological studies
Elastins
Laminins
Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(degradation inhibitors; **skin** prepns. containing plant (exts.) as **matrix metalloprotease** inhibitors)
IT Human
(**matrix metalloproteinases** of; **skin** prepns. containing plant (exts.) as **matrix metalloprotease** inhibitors)
IT Artocarpus elasticus
Cinnamomum iners
Desmodium triquetrum
Equisetum debile
Loranthus
Schima noronhae
Simal (Bombax ceiba)
(**skin** prepns. containing plant (exts.) as **matrix metalloprotease** inhibitors)
IT **9001-12-1**, Collagenase **9040-48-6**, Gelatinase **79955-99-0**, Stromelysin **141907-41-7**, **Matrix metalloprotease 146480-36-6**, **Matrix metalloprotease** 9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**skin** prepns. containing plant (exts.) as **matrix metalloprotease** inhibitors)

L59 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:324077 HCAPLUS
DN 139:193642
ED Entered STN: 29 Apr 2003
TI **Skin** damage and its control on photoaging
AU **Amano, Satoshi**; Nishiyama, Toshio
CS Skin Biology Research Lab., **Shiseido** Life Science Research Center, Yokohama, Kanagawa, 236-8643, Japan
SO Saibo (2003), 35(4), 140-143
CODEN: SAIBC7; ISSN: 1346-7557
PB Nyu Saiensusha
DT Journal; General Review
LA Japanese
CC 8-0 (Radiation Biochemistry)
AB A review, discussing **skin** damage and its control on photoaging with regards to gelatinase and repair of **basement membrane** by **skin**-care products.
ST review **skin** damage photoaging gelatinase
IT **Skin, disease**
(**injury**; **skin** damage and its control on **photoaging**)
IT **Skin, disease**
(**photoaging**; **skin** damage and its control on **photoaging**)
IT Human
(**skin** damage and its control on photoaging)
IT **9040-48-6**, Gelatinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**skin** damage and its control on photoaging)

L59 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:96165 HCAPLUS
DN 138:142206
ED Entered STN: 07 Feb 2003
TI **Skin** vitalizing composition for external use anti-aging preparation
IN **Amano, Satoshi**; Ogura, Yuki; **Matsunaga, Yukiko**; Tsuda, Takanari; Aoyama, Yukari; Koga, Nobuyoshi
PA **Shiseido** Company Limited, Japan
SO Eur. Pat. Appl., 30 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K007-48
CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1281396	A2	20030205	EP 2002-292849	20021115
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2004075661	A2	20040311	JP 2002-323030	20021106
	US 2004001897	A1	20040101	US 2002-314165	20021209
	CN 1465338	A	20040107	CN 2003-100032	20030106
PRAI	JP 2002-177601	A	20020618		
	JP 2002-323030	A	20021106		

AB The invention provides an **epidermal basement membrane** structure formation accelerating preparation and a **skin** external preparation comprising a serine protease inhibitor, and optionally an accelerator of production of extracellular **matrix** protein components of the **epidermal basement membrane.** It also provides, as a means for producing artificial **skin** having an adequately formed **basement membrane**, an artificial **skin**-forming medium which comprises a serine protease inhibitor, and optionally an accelerator of production of extracellular **matrix** protein components of the **epidermal basement membrane** and a **matrix metalloprotease** inhibitor, as well as a method for producing the same.

ST proteinase inhibitor lysophospholipid antiaging cosmetic; **basement membrane skin epidermis** antiaging cosmetic; extracellular matrix protein antiaging cosmetic; **skin** transplant proteinase inhibitor

IT Laminins
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(5; **skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)

IT **Cosmetics**
(antiaging; **skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)

IT **Skin**
(artificial, culturing of; **skin** vitalizing composition for external use antiaging preparation and artificial **skin** containing proteinase inhibitors)

IT **Cosmetics**
(creams; **skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)

IT **Cosmetics**
(emulsions; **skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)

IT **Skin**
(**epidermis, basement membranes,**

accelerators of production of; **skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(extracellular matrix-associated, accelerators of production of; **skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)
IT Mentha
(exts.; **skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)
IT **Cosmetics**
(foundations; **skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)
IT Fagus
(lysophospholipids of; **skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)
IT **Basement membrane**
(**skin epidermis**, accelerators of production of; **skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)
IT Interleukin 1
Lysophospholipids
Platelet-derived growth factors
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(**skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)
IT Transplant and Transplantation
(**skin**; **skin** vitalizing composition for external use antiaging preparation and artificial **skin** containing proteinase inhibitors)
IT Lysophosphatidylcholines
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(soybean; **skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)
IT **Skin**
(transplant; **skin** vitalizing composition for external use antiaging preparation and artificial **skin** containing proteinase inhibitors)
IT Collagens, biological studies
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(type IV; **skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)
IT Collagens, biological studies
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(type VII; **skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)
IT Transforming growth factors
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(α-; **skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)
IT 37259-58-8, Serine protease **141907-41-7**, **Matrix metalloprotease**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)
IT 9087-70-1, Aprotinin 177701-98-3
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);

USES (Uses)
(**skin** vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids)

L59 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:79438 HCAPLUS
DN 138:398112
ED Entered STN: 02 Feb 2003
TI Possible involvement of gelatinases in **basement membrane** damage and wrinkle formation in chronically ultraviolet B-exposed hairless mouse
AU **Inomata, Shinji**; **Matsunaga, Yukiko**; **Amano, Satoshi**; Takada, Keiko; Kobayashi, Kouji; Tsunenaga, Makoto; Nishiyama, Toshio; Kohno, Yoshiyuki; Fukuda, Minoru
CS Skincare Ingredient Research Laboratories, **Shiseido** Life Science Research Center, Yokohama, 224-8558, Japan
SO Journal of Investigative Dermatology (2003), 120(1), 128-134
CODEN: JIDEAE; ISSN: 0022-202X
PB Blackwell Publishing, Inc.
DT Journal
LA English
CC 8-6 (Radiation Biochemistry)
AB A number of studies indicate that **matrix metalloproteinase** might be involved in photoaging, but little is known about their direct contribution to UV-induced histol. and morphol. changes in the **skin** in vivo. This study reports the relationship between changes of **matrix metalloproteinase** activities and UV B-induced **skin** changes in hairless mouse. The role of **matrix metalloproteinase** in the **skin** changes was studied by topical application of a specific **matrix metalloproteinase** inhibitor. The backs of mice were exposed to UV B three times a week for 10 wk. Histol. studies showed that the **basement membrane** structure was damaged, with **epidermal** hyperplasia, in the first 2 wk of UV B irradiation, followed by the appearance of wrinkles, which gradually extended in the latter half of the UV B irradiation period. We observed enhancement of type IV collagen degradation activity, but not collagenase or **matrix metalloproteinase**-3 activity, in exts. of UV B-irradiated, wrinkle-bearing **skin.** Gelatin zymog. anal. revealed that gelatinases, **matrix metalloproteinase**-9 and **matrix metalloproteinase**-2, were significantly increased in the extract In situ zymog. study clarified that the activity was specifically localized in whole **epidermis** of UV B-irradiated, wrinkled **skin** in comparison with normal **skin.** The activity was induced around the basal layer of the **epidermis** by a single UV exposure of at least one minimal erythema dose. Furthermore, topical application of a specific **matrix metalloproteinase** inhibitor, CGS27023A, inhibited UV B-induced gelatinase activity in the **epidermis**, and its repeated application prevented UV B-induced damage to the **basement membrane**, as well as **epidermal** hyperplasia and **dermal** collagen degradation UV B-induced wrinkles were also prevented by administration of the inhibitor. These results, taken together, suggest that UV B-induced enhancement of gelatinase activity in the **skin** contributes to wrinkle formation through the destruction of **basement membrane** structure and **dermal** collagen in chronically UV B-exposed hairless mouse, and thus topical application of **matrix metalloproteinase** inhibitors may be an effective way to prevent UV B-induced wrinkle formation.
ST gelatinase **basement membrane skin** wrinkle formation chronic UVB exposure; photoprotectant **matrix metalloproteinase** inhibitor
IT **Skin, disease**

(**epidermis**, **hyperplasia**; gelatinases involvement in **basement membrane** damage and wrinkle formation in chronic UVB exposure)

IT **Basement membrane**
UV B radiation
(gelatinases involvement in **basement membrane** damage and wrinkle formation in chronic UVB exposure)

IT **Skin, disease**
(**photoaging**, wrinkles; gelatinases involvement in **basement membrane** damage and wrinkle formation in chronic UVB exposure)

IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type IV; gelatinases involvement in **basement membrane** damage and wrinkle formation in chronic UVB exposure)

IT **9001-12-1**, Collagenase **79955-99-0**, **Matrix metalloproteinase**-3 **146480-35-5**, **Matrix metalloproteinase**-2 **146480-36-6**, **Matrix metalloproteinase**-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gelatinases involvement in **basement membrane** damage and wrinkle formation in chronic UVB exposure)

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L59 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:615807 HCAPLUS
DN 137:165826
ED Entered STN: 16 Aug 2002
TI Method of isolating epithelial cells, method of preconditioning cells, and methods of preparing bioartificial skin and dermis with the epithelial cells or the preconditioned cells
IN Son, Young-Sook; Park, Hyun-Sook; Kim, Chun-Ho; Kang, Hyun-Ju; Kim, Chang-Hwan; Kim, Youn-Young; Choi, Young-Ju; Lee, Su-Hyun; Gin, Yong-Jae
PA Korea Atomic Energy Research Institute, S. Korea
SO PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N005-08
CC 9-11 (Biochemical Methods)
Section cross-reference(s): 13, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002062971	A1	20020815	WO 2001-KR1873	20011106 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI KR 2001-5934 A 20010207 <--
KR 2001-47723 A 20010808

AB A method of isolating epithelial cells from a human skin tissue or internal organ tissue using trypsin and EDTA simultaneously with the application of magnetic stirring, a method of preconditioning isolated biol. cells by the application of phys. stimulus, i.e., strain, are provided. Epithelial cells can be isolated by the method with increased yield, colony forming efficiency (CFE), and colony size. Also, the increased percentage of stem cells in isolated cells is advantageous in therapeutic tissue implantation by autologous or allogeneic transplantation. In skin cells preconditioned by the application of strain, cell division is facilitated, and the secretion of extracellular **matrix** components and growth factors and the activity of **matrix metalloproteinases** (**MMPs**) are improved.
When preconditioned cells are implanted by autologous or allogeneic transplantation to heal a damaged tissue, the improved cell adhesion, mobility, and viability provides a biol. adjustment effect against a variety of stresses or phys. stimuli which the cells would undergo after implantation, with improved capability of integration into host tissue, thereby markedly improving the probability of success in skin grafting.

ST epithelial cell isolation trypsin EDTA magnetic stirring; preconditioning skin cell strain; bioartificial skin dermis preconditioned epithelial cell
IT Cyclins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D1; isolating epithelial cells and preconditioning cells and preparing

bioartificial skin and dermis with epithelial cells or preconditioned cells)

IT Arm
(armpit, tissue of; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)

IT Eye
(**artificial** cornea; isolating epithelial cells and preconditioning cells and preparing bioartificial **skin** and dermis with epithelial cells or preconditioned cells)

IT **Skin**
(**artificial**; isolating epithelial cells and preconditioning cells and preparing bioartificial **skin** and dermis with epithelial cells or preconditioned cells)

IT **Epithelium**
(cells of; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)

IT Eye
(cornea, tissue of; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)

IT Eye
(cornea, transplant; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)

IT Transplant and Transplantation
(cornea; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)

IT **Skin**
(dermis; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)

IT Uterus
(endometrium, tissue of; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)

IT Blood vessel
(endothelium, cells of, in bioartificial skin construct; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)

IT Esophagus
Intestine
(epithelium, tissue of; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)

IT Hair
(follicle, cells of, in bioartificial skin construct; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)

IT Hair
(follicle, outer root sheath, in bioartificial skin construct; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)

IT Collagens, biological studies
Fibrins
RL: BUU (Biological use, unclassified); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gelated, solution of; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)

IT Neoplasm
(healing after treatment of; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Radiotherapy
Surgery
(healing after; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Burn
(healing; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Fibroblast
Melanocyte
(in bioartificial skin construct; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Organ, animal, disease
Skin, disease
(**injury**, healing; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(involucrins; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Animal tissue culture
Cell differentiation
Human
Stress, animal
Transplant and Transplantation
Wound healing
Wound healing promoters
(isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Fibronectins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Glycosaminoglycans, biological studies
RL: BUU (Biological use, unclassified); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT **Skin**
(keratinocyte; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Mouth
(mucosa, epithelium, tissue of; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Nose
Stomach
(mucosa, tissue of; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or

preconditioned cells)
IT Stress, animal
(phys.; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Surgery
(plastic, dermatoplastic; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Penis
(prepuce, tissue of; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Collagens, biological studies
Fibrins
RL: BUU (Biological use, unclassified); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solution of; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Mixing
(stirring, magnetic; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Abdomen
Bladder
Hip
Kidney
Mammary gland
Scalp
Skin
Urethra
Vagina
(tissue of; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type IV; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT **Skin, disease**
(**ulcer**, healing; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT 127464-60-2, Vascular endothelial growth factor **146480-35-5**, **Matrix metalloproteinase**-2 **146480-36-6**, **Matrix metalloproteinase**-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT 60-00-4, EDTA, biological studies 9002-07-7, Trypsin
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)
IT 423153-13-3, Integra **Artificial Skin** 447397-66-2, Alloderm 447397-67-3, Terudermis 447397-68-4, Beschitin W
RL: BUU (Biological use, unclassified); TEM (Technical or engineered

material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isolating epithelial cells and preconditioning cells and preparing bioartificial **skin** and dermis with epithelial cells or preconditioned cells)

IT 9012-76-4, Chitosan
RL: BUU (Biological use, unclassified); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neutralized sponge of; isolating epithelial cells and preconditioning cells and preparing bioartificial skin and dermis with epithelial cells or preconditioned cells)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anon; Am J Respir Cell Mol Biol 1994, V10(4), P347
(2) Anon; Cell Adhes Commun 1995, V3(3), P243
(3) Anon; Differentiation 1985, V29(2), P169
(4) Anon; J Invest Dermatol 1978, V70(5), P288
(5) Anon; Lab Invest 1989, V61(3), P350
(6) Anon; Lab Invest 1991, V64(5), P682

L59 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2002:555365** HCAPLUS
DN **137:129555**
ED Entered STN: 26 Jul 2002
TI Cosmetic or pharmaceutical preparations of the treatment of epithelial outer tissue containing peptide-based inhibitors of **matrix-metalloproteinases**
IN Adomat, Christel; Petersohn, Dirk; Foerster, Thomas; Foerster, Matthias
PA Henkel Kommanditgesellschaft auf Aktien, Germany
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM A61K038-00
CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 3, 7, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002056901	A2	20020725	WO 2002-EP379	20020116 <--
	WO 2002056901	A3	20021121		
	W: AU, BG, BR, BY, CA, CN, CZ, DZ, HU, ID, IL, IN, JP, KR, MX, NO, NZ, PL, RO, RU, SG, SI, SK, UA, US, UZ, VN, YU, ZA				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	DE 10102784	A1	20020801	DE 2001-10102784	20010122 <--
PRAI	DE 2001-10102784	A	20010122 <--		

AB The invention relates to cosmetic or pharmaceutical prepns. for the treatment of epithelial outer tissue, comprising peptide-based inhibitors of **matrix-metalloproteinases**, the use of said peptide-based inhibitors of **matrix-metalloproteinases** for the treatment of epithelial outer tissue and hand washing agents, body-care products or hand washing-up liqs., containing said peptide-based inhibitors of **matrix-metalloproteinases.** Thus proteinase inhibitor TIMP-1 was expressed in BL21/DE3 cells, isolated and used in a cream that contained (weight/weight%): diacapryl ether 7.0; dioleate 7.0; behenylalc. 7.0; sodium cetearyl sulfate 0.18; dimethicone 0.5; Vitamin E 1.0; D-panthenol 1.0; glycerol 5.0; TIMP-1 0.01-1; lecithin 2.0; water 69.23-68.24; formalin (37%) 0.05.

ST cosmetic pharmaceutical cream **metalloproteinase** inhibitor TIMP

IT **Epithelium**
Genetic engineering
(cosmetic or pharmaceutical prepns. of treatment of epithelial outer tissue containing peptide-based inhibitors of **matrix-**

metalloproteinases)
IT **Cosmetics**
(creams; cosmetic or pharmaceutical prepns. of treatment of epithelial outer tissue containing peptide-based inhibitors of **matrix-metalloproteinases**)
IT Drug delivery systems
(ointments, creams; cosmetic or pharmaceutical prepns. of treatment of epithelial outer tissue containing peptide-based inhibitors of **matrix-metalloproteinases**)
IT **140208-24-8P**, TIMP-1
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cosmetic or pharmaceutical prepns. of treatment of epithelial outer tissue containing peptide-based **inhibitors** of **matrix-metalloproteinases**)
IT **124861-55-8**, TIMP-2 **145809-21-8**, TIMP-3
186207-03-4, TIMP-4
RL: BSU (Biological study, unclassified); COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cosmetic or pharmaceutical prepns. of treatment of epithelial outer tissue containing peptide-based **inhibitors** of **matrix-metalloproteinases**)
IT **9001-12-1**, **Matrix metalloproteinase**-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors** of; cosmetic or pharmaceutical prepns. of treatment of epithelial outer tissue containing peptide-based **inhibitors** of **matrix-metalloproteinases**)
IT 443817-56-9 443817-57-0 443817-58-1 443817-59-2 443817-60-5
443817-61-6 443817-62-7 443817-63-8
RL: PRP (Properties)
(unclaimed sequence; cosmetic or pharmaceutical prepns. of the treatment of epithelial outer tissue containing peptide-based inhibitors of **matrix-metalloproteinases**)

L59 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:855224 HCAPLUS
DN 136:197396
ED Entered STN: 27 Nov 2001
TI Importance of Balance between Extracellular Matrix Synthesis and Degradation in **Basement Membrane** Formation
AU **Amano, Satoshi**; Akutsu, Nobuko; **Matsunaga, Yukiko**; Kadoya, Kuniko; Nishiyama, Toshio; Champliaud, Marie-France; Burgeson, Robert E.; Adachi, Eijiro
CS **Shiseido** Life Science Research Center, Yokohama, 236-8643, Japan
SO Experimental Cell Research (**2001**), 271(2), 249-262
CODEN: ECREAL; ISSN: 0014-4827
PB Academic Press
DT Journal
LA English
CC 13-2 (Mammalian Biochemistry)
AB The **epidermal basement membrane** (BM) plays important roles in adhesion between **epidermis** and **dermis** and in controlling **epidermal** differentiation. In a **skin**-equivalent (SE), components of the **epidermal** BM such as laminin 5 and type IV and VII collagens were detected in conditioned media and in basal keratinocytes. Despite production of these BM components, however, BM was rarely observed at the **dermal-epidermal** junction. One possible explanation for the absence of BM in SEs is that **matrix metalloproteinases** (**MMPs**) degrade newly synthesized extracellular **matrixes**. In fact, several **MMPs**, such as **MMPs**-1, 2, 3, and 9, were observed to be present in conditioned media and some of them were in active forms.

Tissue inhibitor of **metalloproteinase** (TIMP)-2 was not detected, although TIMP-1 was present. BM degradation activity presumably exceeds BM formation activity in the SE, resulting in the absence of lamina densa at the **dermal-epidermal** junction. Synthetic **MMP** inhibitors CGS27023A and **MMP** inhibitor I, which inhibit **MMPs** 1, 2, 3, and 9, markedly augmented deposition of laminin 5 and type IV and VII collagens at the **dermal-epidermal** junction, resulting in formation of continuous **epidermal** BM. These results suggest that the balance between synthesis and degradation of BM components is important for BM formation. (c) 2001 Academic Press.

ST laminin collagen **metalloproteinase** extracellular **matrix** formation **basement membrane epidermis**

IT Laminins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(5; balance between synthesis of extracellular **matrix** components and their degradation by **matrix metalloproteinases** in **basement membrane** formation at **dermal-epidermal** junction)

IT **Basement membrane**
Extracellular **matrix**
(balance between synthesis of extracellular **matrix** components and their degradation by **matrix metalloproteinases** in **basement membrane** formation at **dermal-epidermal** junction)

IT **Skin**
(**dermis**; balance between synthesis of extracellular **matrix** components and their degradation by **matrix metalloproteinases** in **basement membrane** formation at **dermal-epidermal** junction)

IT **Skin**
(**epidermis**; balance between synthesis of extracellular **matrix** components and their degradation by **matrix metalloproteinases** in **basement membrane** formation at **dermal-epidermal** junction)

IT **Skin**
(keratinocyte; balance between synthesis of extracellular **matrix** components and their degradation by **matrix metalloproteinases** in **basement membrane** formation at **dermal-epidermal** junction)

IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type IV; balance between synthesis of extracellular **matrix** components and their degradation by **matrix metalloproteinases** in **basement membrane** formation at **dermal-epidermal** junction)

IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type VII; balance between synthesis of extracellular **matrix** components and their degradation by **matrix metalloproteinases** in **basement membrane** formation at **dermal-epidermal** junction)

IT **9001-12-1**, **Matrix metalloproteinase**-1 **79955-99-0**, **Matrix metalloproteinase**-3 **140208-24-8**, TIMP-1 **146480-35-5**, **Matrix metalloproteinase**-2 **146480-36-6**, **Matrix metalloproteinase**-9 **148969-98-6**, Promatrix **metalloproteinase**-2 **152787-66-1**, Promatrix **metalloproteinase**-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(balance between synthesis of extracellular **matrix** components and their degradation by **matrix metalloproteinases** in **basement membrane** formation at **dermal-epidermal** junction)

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L59 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:732793 HCAPLUS
DN 136:18487
ED Entered STN: 08 Oct 2001
TI Reconstruction of **basement membrane** in **skin** equivalent; Role of laminin-1
AU Yi, Jae Youn; Yoon, Yong Ha; Park, Hyun Sook; Kim, Chun Ho; Kim, Chang Hwan; Kang, Hyun Joo; Lee, EunAh; Kim, Youn Young; Jin, Yong Jae; Kim, Tae Hwan; Son, Young Sook
CS Laboratory of Tissue Engineering, Korea Cancer Center Hospital, Seoul, 139-706, S. Korea
SO Archives of Dermatological Research (**2001**), 293(7), 356-362
CODEN: ADREDL; ISSN: 0340-3696
PB Springer-Verlag

DT Journal
LA English
CC 13-6 (Mammalian Biochemistry)
Section cross-reference(s): 63
AB To reconstruct the **basement membrane** in a **skin** equivalent, the **epidermodermal** interface was coated with porcine type IV collagen and mouse laminin-1 at various ratios before keratinocyte seeding. Laminin-1, a component of the **basement membrane**, induced massive infiltration of keratinocytes into the **dermal** equivalent, while type IV collagen induced discrete demarcation between **dermal** and **epidermal** compartments without any infiltrating cells. Immunohistochem. staining indicated that the laminin-induced infiltrating cells expressed endogenous type IV collagens at the cell periphery, which were not incorporated into the **basement membrane** structure. The infiltrating cells did not express fibronectin receptor α5β1 integrin but showed **MMP**-9 secretion and cell surface associated **MMP**-2. However, when laminin-1 was preincubated with type IV collagen, laminin-1-induced keratinocyte infiltration as well as **MMP**-9 induction were almost completely suppressed to basal levels. Therefore, replenishment of the type IV collagen lattice seemed to cause laminin-stimulated cells to anchor to the lattice, in a similar manner to the basal cells on the **basement membrane** of normal **skin.** Our study suggests that the molar ratio of **basement membrane** components may determine the behavior of basal cells within the wound healing microenvironment, which is probably regulated either by extracellular matrix deposition or degradation
ST laminin **basement membrane** reconstruction **artificial skin**
IT Laminins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(1; role of laminin-1 in reconstruction of **basement membrane** in **skin** equivalent)
IT **Skin**
(**artificial**; role of laminin-1 in reconstruction of **basement membrane** in **skin** equivalent)
IT **Skin**
(keratinocyte; role of laminin-1 in reconstruction of **basement membrane** in **skin** equivalent)
IT **Basement membrane**
Cell migration
Wound healing
(role of laminin-1 in reconstruction of **basement membrane** in **skin** equivalent)
IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type IV; role of laminin-1 in reconstruction of **basement membrane** in **skin** equivalent)
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α5β1; role of laminin-1 in reconstruction of **basement membrane** in **skin** equivalent)
IT **146480-35-5, MMP 2 146480-36-6, MMP 9**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role of laminin-1 in reconstruction of **basement membrane** in **skin** equivalent)
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L59 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2001:717824** HCAPLUS
DN **135:278068**
ED Entered STN: 02 Oct 2001
TI **Skin basement membrane** formation promoters containing **matrix metalloprotease** inhibitors and manufacture of **artificial skin** using the promoters
IN **Amano, Satoshi; Matsunaga, Yukiko; Inomata, Shinji**
PA **Shiseido** Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 17 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61L027-00
ICS A61K045-00; A61K045-06; A61P017-00
CC 63-7 (Pharmaceuticals)
Section cross-reference(s): 62
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2001269398	A2	20011002	JP 2000-87574	20000327 <--
	WO 2001072347	A1	20011004	WO 2001-JP2507	20010327 <--
	W: CN, KR, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	EP 1180371	A1	20020220	EP 2001-915860	20010327 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 2002193875	A1	20021219	US 2001-979712	20011126 <--
	US 2004038859	A1	20040226	US 2003-648485	20030827 <--
PRAI	JP 2000-87574	A	20000327 <--		
	WO 2001-JP2507	W	20010327 <--		
	US 2001-979712	A1	20011126 <--		

AB **Skin basement membrane** formation promoters and **artificial skin** formation promoters contain **matrix metalloprotease** inhibitors and optionally **matrix** protein production promoters. **Artificial**

skin is manufactured by adding **matrix metalloprotease** inhibitors and optionally **matrix** protein production promoters to a medium for **artificial skin** manufacture A **skin** model having stratified **epidermis**, obtained by culturing human foreskin-derived **epidermal** keratinocyte on contracted collagen gel, was further cultured in a medium containing CGS 27023A for 2 wk to form **basement membrane** structure. Plant exts., e.g those of Thymus serpyllum, Potentilla tormentilla, Thea sinensis, etc., had a similar effect. Cosmetic formulations containing the **basement membrane** formation promoters were also given.

ST **skin basement membrane** formation promoter **matrix metalloprotease** inhibitor; protein **matrix** prodn promoter **skin basement membrane** formation; **artificial skin** manuf **matrix metalloprotease** inhibitor

IT **Skin**
(**artificial**; **skin basement membrane** formation promoters containing **matrix metalloprotease** inhibitors and optionally **matrix** protein production promoters for manufacture of **artificial skin**)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(**matrix**, production promoters for; **skin basement membrane** formation promoters containing **matrix metalloprotease** inhibitors and optionally **matrix** protein production promoters for manufacture of **artificial skin**)

IT **Basement membrane**
(**skin basement membrane** formation promoters containing **matrix metalloprotease** inhibitors and optionally **matrix** protein production promoters for manufacture of **artificial skin**)

IT Collagens, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**skin basement membrane** formation promoters containing **matrix metalloprotease** inhibitors and optionally **matrix** protein production promoters for manufacture of **artificial skin**)

IT Lysophosphatidylcholines
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soybean; **skin basement membrane** formation promoters containing **matrix metalloprotease** inhibitors for manufacture of **artificial skin**)

IT Transforming growth factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α-; **skin basement membrane** formation promoters containing **matrix metalloprotease** inhibitors for manufacture of **artificial skin**)

IT Transforming growth factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β1-; **skin basement membrane** formation promoters containing **matrix metalloprotease** inhibitors for manufacture of **artificial skin**)

IT **141907-41-7**
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**inhibitors**; **skin basement membrane** formation promoters containing **matrix metalloprotease inhibitors** and optionally **matrix** protein production promoters for manufacture of **artificial skin**)

IT 124168-73-6 169799-04-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**skin basement membrane** formation promoters containing **matrix metalloprotease** inhibitors and optionally **matrix** protein production promoters for manufacture of **artificial skin**)

L59 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2000:834192** HCAPLUS
DN **134:114152**
ED Entered STN: 29 Nov 2000
TI **Basement membrane** alterations in psoriasis are accompanied by **epidermal** overexpression of **MMP**-2 and its inhibitor TIMP-2
AU Fleischmajer, Raul; Kuroda, Kei; Hazan, Rachel; Gordon, Ronald E.; Lebwohl, Mark G.; Sapadin, Allen N.; Unda, Fernando; Iehara, Noriyuki; Yamada, Yoshihiko
CS Department of Dermatology, Mount Sinai Medical Center, New York, NY, 10029, USA
SO Journal of Investigative Dermatology (**2000**), 115(5), 771-777
CODEN: JIDEAE; ISSN: 0022-202X
PB Blackwell Science, Inc.
DT Journal
LA English
CC 14-9 (Mammalian Pathological Biochemistry)
AB Psoriasis is most probably an inherited disease characterized by cell proliferation, angiogenesis, and an inflammatory process. The pathophysiol. remains unknown, although an alteration in cell-cell and cell-**matrix** adhesion vs. an autoimmune process has been proposed as the primary defect. Here, the authors show evidence of a new mechanism involving **basement membrane** alterations accompanied by keratinocyte overexpression of **matrix metalloproteinase** (**MMP**) 2 and tissue inhibitor of **MMP**-2 (TIMP-2) in both uninvolved and involved psoriatic **skin.** Immunocytochem. with antibodies against collagen IV (α1, α2 chains) and laminins (α2, α5, β1, γ1 chains) revealed gaps, folding, and reduplication of the **epidermo-dermal basement membrane.** There was overexpression of **MMP**-2 in the cytoplasm of suprabasal keratinocytes. Gelatin zymog. revealed pro-**MMP**-2 and its activated form, a-**MMP**-2, in both uninvolved and involved psoriatic **skin**, whereas pro-**MMP** -9 was only present in involved **skin.** TIMP-2 was expressed at the cell surface of psoriatic involved suprabasal keratinocytes whereas it was restricted to basal keratinocytes in uninvolved areas. Western blots showed a marked increase in a-**MMP**-2 and TIMP-2 in uninvolved and involved psoriatic **skin** although it was more pronounced in the latter. MT1-**MMP**, known to activate pro-**MMP**-2, was increased in involved areas. In situ hybridization revealed strong signals of **MMP**-2 mRNA in both uninvolved and involved psoriatic **epidermis.** The overexpression of **MMP**-2 in uninvolved and involved psoriatic **epidermis** supports the concept that the primary alteration may reside in the keratinocyte. In addition, the presence of the activated form of **MMP**-2 could be responsible for cell-cell and cell-**matrix** changes noted in psoriatic **epidermis.**
ST **epidermal** overexpression **MMP2** TIMP2 psoriasis

basement membrane alteration
IT Transcription, genetic
(**MMP**-2 gene; **basement membrane** alterations in psoriasis are accompanied by **epidermal** overexpression of **MMP**-2 and inhibitor TIMP-2 in humans)
IT Cytoplasm
(**MMP**-2 in; **basement membrane** alterations in psoriasis are accompanied by **epidermal** overexpression of **MMP**-2 and inhibitor TIMP-2 in humans)
IT Gene, animal
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**MMP**-2; **basement membrane** alterations in psoriasis are accompanied by **epidermal** overexpression of **MMP**-2 and inhibitor TIMP-2 in humans)
IT mRNA
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(**MMP**-2; **basement membrane** alterations in psoriasis are accompanied by **epidermal** overexpression of **MMP**-2 and inhibitor TIMP-2 in humans)
IT Cell **membrane**
(TIMP-2 on; **basement membrane** alterations in psoriasis are accompanied by **epidermal** overexpression of **MMP**-2 and inhibitor TIMP-2 in humans)
IT **Skin**
(basal cell; **basement membrane** alterations in psoriasis are accompanied by **epidermal** overexpression of **MMP**-2 and inhibitor TIMP-2 in humans)
IT **Basement membrane**
Psoriasis
(**basement membrane** alterations in psoriasis are accompanied by **epidermal** overexpression of **MMP**-2 and inhibitor TIMP-2 in humans)
IT Laminins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**basement membrane** alterations in psoriasis are accompanied by **epidermal** overexpression of **MMP**-2 and inhibitor TIMP-2 in humans in relation to)
IT **Skin**
(keratinocyte; **basement membrane** alterations in psoriasis are accompanied by **epidermal** overexpression of **MMP**-2 and inhibitor TIMP-2 in humans)
IT Collagens, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(type IV; **basement membrane** alterations in psoriasis are accompanied by **epidermal** overexpression of **MMP**-2 and inhibitor TIMP-2 in humans in relation to)
IT **124861-55-8**, Proteinase **inhibitor**, TIMP-2
146480-35-5, Gelatinase A **148969-98-6**, Pro-**MMP**-2
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**basement membrane** alterations in psoriasis are accompanied by **epidermal** overexpression of **MMP**-2 and **inhibitor** TIMP-2 in humans)
IT **161384-17-4**, MT1-**MMP**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or

effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**basement membrane** alterations in psoriasis are accompanied by **epidermal** overexpression of **MMP**-2 and **inhibitor** TIMP-2 in humans in relation to)

IT **152787-66-1**, Pro-**MMP**-9
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**basement membrane** alterations in psoriasis are accompanied by **epidermal** overexpression of **MMP**-2 and **inhibitor** TIMP-2 in humans in relation to)

RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD

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AN 2000:535884 HCAPLUS
DN 133:263089
ED Entered STN: 06 Aug 2000
TI Bone morphogenetic protein 1 is an extracellular processing enzyme of the laminin 5 γ2 chain
AU **Amano, Satoshi**; Scott, Ian C.; Takahara, Kazuhiko; Koch, Manuel; Champliaud, Marie-France; Gerecke, Donald R.; Keene, Douglas R.; Hudson, David L.; Nishiyama, Toshio; Lee, Seungbok; Greenspan, Daniel S.; Burgeson, Robert E.
CS MGH/Harvard Cutaneous Biology Research Center, Massachusetts General Hospital, Charlestown, MA, 02129, USA
SO Journal of Biological Chemistry (**2000**), 275(30), 22728-22735
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 7-3 (Enzymes)
Section cross-reference(s): 13
AB Epithelial cells maintained in culture medium containing low calcium proteolytically process laminin 5 (α3β3γ2) within the α3 and γ2 chains. Expts. were designed to identify the enzyme(s) responsible for the laminin 5 processing and the sites of proteolytic cleavage. To characterize the nature of laminin 5 processing, we determined the N-terminal amino acid sequences of the proteolytic fragments produced by the processing events. The results indicate that the first α3 chain cleavage (200-165 kDa α3) occurs within subdomain G4 of the G domain. The second cleavage (165-145 kDa α3) occurs within the IIIa domain, 11 residues N-terminal to the start of domain II. The γ chain is cleaved within the second **epidermal** growth factor-like repeat of domain III. The sequence cleaved within the γ2 chain matches the consensus sequence for the cleavage of type I, II, and III procollagens by bone morphogenetic protein-1 (BMP-1), also known as type I procollagen C-proteinase. Recombinant BMP-1 cleaves γ2 in vitro, both within intact laminin 5 and at the predicted site of a recombinant γ2 short arm. α3 Is also cleaved by BMP-1 in vitro, but the cleavage site is yet to be determined These results show the laminin α3 and γ2 chains to be substrates for BMP-1 in vitro. We speculate that γ2 cleavage is required for formation of the laminin 5-6 complex and that this complex is directly involved in assembly of the interhemidesmosomal **basement membrane.** This further suggests that BMP-1 activity facilitates **basement membrane** assembly, but not hemidesmosome assembly, in the laminin 5-rich **dermal-epidermal** junction **basement membrane** in vivo.
ST lamin 5 processing bone morphogenetic protein 1
IT Laminins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(5; bone morphogenetic protein 1 is an extracellular processing enzyme of the laminin 5 γ2 chain)
IT Post-translational processing
(bone morphogenetic protein 1 is an extracellular processing enzyme of the laminin 5 γ2 chain)
IT **Skin**
(keratinocyte; bone morphogenetic protein 1 is an extracellular processing enzyme of the laminin 5 γ2 chain)
IT 9005-49-6, Heparin, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(bone morphogenetic protein 1 is an extracellular processing enzyme of the laminin 5 γ2 chain)

IT **68651-95-6**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(bone morphogenetic protein 1; bone morphogenetic protein 1 is an extracellular processing enzyme of the laminin 5 γ2 chain)

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD

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AN **2000:456916** HCAPLUS
DN **133:68929**
ED Entered STN: 07 Jul 2000
TI Use of a **matrix metalloproteinase** inhibitor and an integrin antagonist in the treatment of neoplasia

IN McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PA G.D. Searle and Co., USA
SO PCT Int. Appl., 358 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K041-00
ICS A61P035-00; A61K045-06
CC 1-6 (Pharmacology)
FAN.CNT 19

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2000038719	A1	20000706	WO 1999-US30700	19991222	<--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	CA 2356402	AA	20000706	CA 1999-2356402	19991222	<--
	EP 1140183	A1	20011010	EP 1999-968942	19991222	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
	TR 200102499	T2	20011221	TR 2001-20010249919991222		<--
	JP 2002533407	T2	20021008	JP 2000-590670	19991222	<--
	ZA 2001005055	A	20020920	ZA 2001-5055	20010620	<--
	ZA 2001005120	A	20020107	ZA 2001-5120	20010621	<--
PRAI	US 1998-113786P	P	19981223	<--		
	WO 1999-US30700	W	19991222	<--		

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a **matrix metalloproteinase** inhibitor, an integrin antagonist, and an antineoplastic agent.
ST **metalloproteinase** inhibitor integrin antagonist neoplasia antitumor
IT Reproductive organ
(Bartholin's gland, carcinoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(Ewing's sarcoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Vitaxin; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(Wilms' tumor; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Kidney, neoplasm
Kidney, neoplasm
(Wilms', inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT **Keratosis**
(actinic; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(adenocarcinoma; **matrix metalloproteinase** inhibitor

and integrin antagonist in neoplasia treatment)
IT Liver, neoplasm
(adenoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Astrocyte
Astrocyte
(astrocytoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(astrocytoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT **Skin, neoplasm**
Skin, neoplasm
(**basal cell carcinoma**, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(basal cell carcinoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(bladder carcinoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(bronchi carcinoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Mammary gland
(carcinoma, inhibitors, metastasis; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Bladder
Bladder
Bronchi
Bronchi
Ovary, neoplasm
Ovary, neoplasm
(carcinoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Mammary gland
(carcinoma, metastasis, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(carcinoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(carcinosarcoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Musculoskeletal diseases
(cartilage chondrosarcoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Uterus, neoplasm
Uterus, neoplasm
(cervix, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(cervix; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Biliary tract
Biliary tract
(cholangioma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents

(cholangioma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Cartilage
Cartilage
(chondrosarcoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(chondrosarcoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(choroid plexus papilloma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Meninges
(choroid plexus, carcinoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Meninges
Meninges
(choroid plexus, papilloma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Intestine, neoplasm
Intestine, neoplasm
(colon, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(colon; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(digestive tract; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Uterus, disease
(endometrium, hyperplasia; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Blood vessel, neoplasm
(endothelioma, hemangioendothelioma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Hyperplasia
(focal nodular; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Neoplasm
(gastrinoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(germinoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Neuroglia
Neuroglia
(glioblastoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(glioblastoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Pancreatic islet of Langerhans
Pancreatic islet of Langerhans
(glucagonoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(glucagonoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(head; **matrix metalloproteinase** inhibitor and

integrin antagonist in neoplasia treatment)
IT Blood vessel, neoplasm
(hemangioblastoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Blood vessel, neoplasm
Blood vessel, neoplasm
(hemangioma, inhibitors, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(hemangioma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Liver, disease
(hepatic adenomatosis; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Liver, neoplasm
Liver, neoplasm
(hepatoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(hepatoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Lung, neoplasm
(inhibitors, metastasis; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Lung, neoplasm
Lung, neoplasm
(inhibitors, pulmonary blastoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Adenoma
Lung, neoplasm
Lung, neoplasm
Pancreas, neoplasm
Pancreas, neoplasm
(inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Pancreatic islet of Langerhans
Pancreatic islet of Langerhans
(insulinoma, inhibitors, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(insulinoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(leiomyosarcoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(lentigo maligna melanoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(lung small-cell carcinoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(lung, metastasis; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
Antitumor agents
(lung, pulmonary blastoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents

Antitumor agents
(lung; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(mammary gland carcinoma, metastasis; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(mammary gland; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Angiogenesis inhibitors
Antitumor agents
Carcinoid
Drug interactions
Radiotherapy
(**matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Thymus gland
(medulla, epithelium, medulloepithelioma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Brain, neoplasm
Brain, neoplasm
(medulloblastoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(medulloblastoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(melanoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(meninges; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT **Mesothelium**
Mesothelium
(mesothelioma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(mesothelioma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Lung, neoplasm
(metastasis, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(metastasis; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT **Skin, neoplasm**
Skin, neoplasm
(mucoepidermoid **carcinoma**, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(mucoepidermoid carcinoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(multiple myeloma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(neck; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Capillary vessel

Pituitary gland
(neoplasia, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Digestive tract
Digestive tract
Head
Head
Mammary gland
Mammary gland
Meninges
Meninges
Neck, anatomical
Neck, anatomical
(neoplasm, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Nerve, neoplasm
Nerve, neoplasm
(neuroblastoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(neuroblastoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Nervous system
(neuroepithelium, neuroepithelial adenocarcinoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Neuroglia
Neuroglia
(oligodendroglioma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(oligodendroglioma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Bone, neoplasm
Bone, neoplasm
(osteosarcoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(osteosarcoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(ovary carcinoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
Antitumor agents
(pancreas; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(pinealoma inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Pineal gland
Pineal gland
(pinealoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Kidney, neoplasm
Kidney, neoplasm
(renal cell carcinoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(renal cell carcinoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)

IT Eye, neoplasm
Eye, neoplasm
(retinoblastoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(retinoblastoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(rhabdomyosarcoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(sarcoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Lung, neoplasm
Lung, neoplasm
(small-cell carcinoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(soft tissue, carcinoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Animal tissue
Animal tissue
(soft, neoplasm, inhibitors, carcinoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Pancreatic islet of Langerhans
(somatostatinoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(squamous cell carcinoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Drug interactions
(synergistic; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Antitumor agents
(uvea melanoma; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT Eye, neoplasm
Eye, neoplasm
(uvea, melanoma, inhibitors; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT 192329-42-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AG 3340; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT 191537-76-5, D 2163
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(D 2163; **matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)
IT 50-18-0, Cyclophosphamide 51-21-8, 5-Fluorouracil 52-24-4, Thiotepa 57-22-7, Vincristine 58-05-9, Leucovorin 76-43-7 128-13-2, Ursodeoxycholic acid 154-93-8, BCNU 302-79-4, Retinoic acid 471-34-1, Calcium carbonate, biological studies 865-21-4, Vinblastine 1464-42-2, Selenomethionine 3562-63-8, Megestrol 7782-49-2, Selenium, biological studies 10540-29-1, Tamoxifen 14769-73-4, Levamisole 15663-27-1, Cisplatin 15866-90-7, CMT 3 23214-92-8, Doxorubicin 33069-62-4, Paclitaxel 33419-42-0, Etoposide 41575-94-4, Carboplatin

59973-80-7, Sulindac sulfone 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 65807-02-5, Goserelin 70052-12-9, Eflornithine 71486-22-1, Vinorelbine 84449-90-1, Raloxifene 89778-26-7, Toremifene 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 112809-51-5, Letrozole 114977-28-5, Docetaxel 120511-73-1, Anastrozole 123948-87-8, Topotecan 154039-60-8, BB-2516 154361-50-9, Capecitabine 175529-44-9 179545-77-8, Bay-12-9566 188968-51-6, EMD-121974 193532-75-1 197791-17-6 197791-77-8 198192-90-4 198194-11-5 204452-33-5 206989-45-9 206989-53-9 206989-60-8 206989-67-5 221900-22-7 221900-36-3 226388-60-9 226388-66-5 226389-91-9 226395-57-9 226395-66-0 226395-67-1 226395-93-3 226396-02-7 226396-03-8 226396-26-5 227751-60-2 243640-62-2 279221-20-4 279221-21-5 279221-22-6 279221-23-7 279221-24-8 279221-25-9 279221-26-0 279221-27-1 279221-28-2 280105-12-6 280105-13-7 280105-14-8 280105-15-9 280105-16-0 280105-17-1 280105-18-2 280105-19-3 280105-20-6 280105-21-7 280105-22-8 280105-23-9 280105-24-0 280105-25-1 280105-26-2 280105-27-3 280105-28-4 280105-29-5 280105-30-8 280105-31-9 280123-02-6 280123-03-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**matrix metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)

IT **141907-41-7**, **Matrix metalloproteinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**matrix metalloproteinase inhibitor** and integrin antagonist in neoplasia treatment)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Alcon Lab Inc; WO 9741844 A 1997 HCAPLUS
(2) Chapman, K; US 5672583 A 1997 HCAPLUS
(3) Cousins, R; WO 9814192 A 1998 HCAPLUS
(4) Glaxo Group Ltd; WO 9748685 A 1997 HCAPLUS
(5) Hagmann, W; US 5629343 A 1997 HCAPLUS

L59 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2000:456915** HCAPLUS
DN **133:84242**
ED Entered STN: 07 Jul 2000
TI Method of using a **matrix metalloproteinase** inhibitor and one or more antineoplastic agents as a combination therapy in the treatment of neoplasia
IN McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PA G.D. Searle and Co., USA
SO PCT Int. Appl., 277 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K041-00
ICS A61P035-00; A61K045-06
CC 1-6 (Pharmacology)
FAN.CNT 19

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000038718	A2	20000706	WO 1999-US30699	19991222 <--
WO 2000038718	A3	20001109		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,

AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2356929 AA 20000706 CA 1999-2356929 19991222 <--
EP 1140182 A2 20011010 EP 1999-968941 19991222 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
TR 200102499 T2 20011221 TR 2001-20010249919991222 <--
JP 2002533406 T2 20021008 JP 2000-590669 19991222 <--
ZA 2001005055 A 20020920 ZA 2001-5055 20010620 <--
ZA 2001005120 A 20020107 ZA 2001-5120 20010621 <--
PRAI US 1998-113786P P 19981223 <--
WO 1999-US30699 W 19991222 <--

AB Methods are provided for the prevention and treatment of neoplasia disorders in a mammal using a combination of a **matrix metalloproteinase** inhibitor and an antineoplastic agent.

ST **matrix metalloproteinase** inhibitor antitumor combination

IT Reproductive organ
(Bartholin's gland, carcinoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Antitumor agents
(Ewing's sarcoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Antitumor agents
(Wilms' tumor; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Kidney, neoplasm
Kidney, neoplasm
(Wilms', inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT **Keratosis**
(actinic; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Antitumor agents
(adenocarcinoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Liver, neoplasm
(adenoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Astrocyte
Astrocyte
(astrocytoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Antitumor agents
(astrocytoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT **Skin, neoplasm**
Skin, neoplasm
(**basal cell carcinoma**, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Antitumor agents
(basal cell carcinoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Antitumor agents

(bladder carcinoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(bronchi carcinoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Bladder
Bladder
Bronchi
Bronchi
(carcinoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(carcinoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(carcinosarcoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Musculoskeletal diseases
(cartilage chondrosarcoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Uterus, neoplasm
Uterus, neoplasm
(cervix, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(cervix; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Biliary tract
Biliary tract
(cholangioma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(cholangioma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Cartilage
Cartilage
(chondrosarcoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(chondrosarcoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(choroid plexus papilloma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Meninges
(choroid plexus, carcinoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Meninges
Meninges
(choroid plexus, papilloma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Intestine, neoplasm
Intestine, neoplasm

(colon, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(colon; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(digestive tract; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Uterus, disease
(endometrium, hyperplasia; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Blood vessel, neoplasm
(endothelioma, hemangioendothelioma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Hyperplasia
(focal nodular; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Neoplasm
(gastrinoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(germinoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Neuroglia
Neuroglia
(glioblastoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(glioblastoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Pancreatic islet of Langerhans
Pancreatic islet of Langerhans
(glucagonoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(glucagonoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(head; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Blood vessel, neoplasm
(hemangioblastoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Blood vessel, neoplasm
Blood vessel, neoplasm
(hemangioma, inhibitors, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(hemangioma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Liver, disease
(hepatic adenomatosis; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia

treatment)
IT Liver, neoplasm
Liver, neoplasm
(hepatoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(hepatoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Lung, neoplasm
Lung, neoplasm
(inhibitors, pulmonary blastoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Adenoma
Lung, neoplasm
Lung, neoplasm
Pancreas, neoplasm
Pancreas, neoplasm
(inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Pancreatic islet of Langerhans
Pancreatic islet of Langerhans
(insulinoma, inhibitors, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(insulinoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(leiomyosarcoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(lentigo maligna melanoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(lung small-cell carcinoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
Antitumor agents
(lung, pulmonary blastoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
Antitumor agents
(lung; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(mammary gland; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
Carcinoid
Drug interactions
Radiotherapy
(**matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Thymus gland
(medulla, epithelium, medulloepithelioma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Brain, neoplasm
Brain, neoplasm
(medulloblastoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(medulloblastoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(melanoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(meninges; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT **Mesothelium**
Mesothelium
(mesothelioma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(mesothelioma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(metastasis; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT **Skin, neoplasm**
Skin, neoplasm
(mucoepidermoid **carcinoma**, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(mucoepidermoid carcinoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(multiple myeloma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(neck; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Capillary vessel
Pituitary gland
(neoplasia, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Digestive tract
Digestive tract
Head
Head
Mammary gland
Mammary gland
Meninges
Meninges
Neck, anatomical
Neck, anatomical
(neoplasm, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Nerve, neoplasm
Nerve, neoplasm
(neuroblastoma, inhibitors; **matrix metalloproteinase**

inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Antitumor agents
(neuroblastoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Nervous system
(neuroepithelium, neuroepithelial adenocarcinoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Neuroglia
Neuroglia
(oligodendroglioma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Antitumor agents
(oligodendroglioma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Bone, neoplasm
Bone, neoplasm
(osteosarcoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Antitumor agents
(osteosarcoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Antitumor agents
Antitumor agents
(pancreas; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Antitumor agents
(pinealoma inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Pineal gland
Pineal gland
(pinealoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Kidney, neoplasm
Kidney, neoplasm
(renal cell carcinoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Antitumor agents
(renal cell carcinoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Eye, neoplasm
Eye, neoplasm
(retinoblastoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Antitumor agents
(retinoblastoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Antitumor agents
(rhabdomyosarcoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Antitumor agents
(sarcoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)

IT Lung, neoplasm
Lung, neoplasm
(small-cell carcinoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(soft tissue, carcinoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Animal tissue
Animal tissue
(soft, neoplasm, inhibitors, carcinoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Pancreatic islet of Langerhans
(somatostatinoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(squamous cell carcinoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Antitumor agents
(uvea melanoma; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT Eye, neoplasm
Eye, neoplasm
(uvea, melanoma, inhibitors; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT 192329-42-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AG 3340; **matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT 52-24-4, Thiotepa 58-05-9, Leucovorin 76-43-7 128-13-2, Ursodeoxycholic acid 302-79-4, Retinoic acid 471-34-1, Calcium carbonate, biological studies 1464-42-2, Selenomethionine 3562-63-8, Megestrol 7782-49-2, Selenium, biological studies 14769-73-4, Levamisole 15663-27-1, Cisplatin 15866-90-7, CMT-3 23214-92-8, Doxorubicin 33069-62-4, Paclitaxel 59973-80-7, Sulindac sulfone 65277-42-1, Ketoconazole 65807-02-5, Goserelin 70052-12-9, Eflornithine 71486-22-1, Vinorelbine 84449-90-1, Raloxifene 89778-26-7, Toremifene 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 112809-51-5, Letrozole 114977-28-5, Docetaxel 120511-73-1, Anastrozole 123948-87-8, Topotecan 154039-60-8, BB-2516 154361-50-9, Capecitabine 179545-77-8, Bay-12-9566 191537-76-5, D 2163 226388-60-9 226388-66-5 226389-91-9 226395-57-9 226395-66-0 226395-67-1 226395-93-3 226396-02-7 226396-03-8 226396-26-5 227619-96-7 279221-20-4 279221-21-5 279221-22-6 279221-23-7 279221-24-8 279221-25-9 279221-26-0 279221-27-1 279221-28-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**matrix metalloproteinase** inhibitor and antineoplastic agent as combination therapy in neoplasia treatment)
IT **141907-41-7, Matrix metalloproteinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**matrix metalloproteinase inhibitor** and antineoplastic agent as combination therapy in neoplasia treatment)

L59 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

AN **2000:441655** HCAPLUS
DN **133:68922**
ED Entered STN: 30 Jun 2000
TI Method of using a cyclooxygenase-2 inhibitor and a **matrix metalloproteinase** inhibitor as a combination therapy in the treatment of neoplasia
IN McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PA G.D. Searle and Co., USA
SO PCT Int. Appl., 437 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K045-06
ICS A61P035-00; A61K041-00
CC 1-6 (Pharmacology)
FAN.CNT 19

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2000037107	A2	20000629	WO 1999-US30776	19991222	<--
	WO 2000037107	A3	20010201			
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	CA 2356426	AA	20000629	CA 1999-2356426	19991222	<--
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	TR 200102499	T2	20011221	TR 2001-20010249	19991222	<--
	BR 9916536	A	20020102	BR 1999-16536	19991222	<--
	JP 2002532563	T2	20021002	JP 2000-589217	19991222	<--
	ZA 2001005055	A	20020920	ZA 2001-5055	20010620	<--
	ZA 2001005120	A	20020107	ZA 2001-5120	20010621	<--
	NO 2001003156	A	20010823	NO 2001-3156	20010622	<--
PRAI	US 1998-113786P	P	19981223 <--			
	WO 1999-US30776	W	19991222 <--			

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a cyclooxygenase-2 inhibitor, a **matrix metalloproteinase** inhibitor and an antineoplastic agent.
ST cyclooxygenase 2 inhibitor **matrix metalloproteinase** inhibitor antitumor combination; COX2 inhibitor **matrix metalloproteinase** inhibitor antitumor combination
IT Reproductive organ
(Bartholin's gland, carcinoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(Ewing's sarcoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(Wilms' tumor; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Kidney, neoplasm
Kidney, neoplasm
(Wilms', inhibitors; cyclooxygenase-2 inhibitor and **matrix**

metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Keratosis**
(actinic; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Antitumor agents
(adenocarcinoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Liver, neoplasm
(adenoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Astrocyte
Astrocyte
(astrocytoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Antitumor agents
(astrocytoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT **Skin, neoplasm**
Skin, neoplasm
(**basal cell carcinoma**, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Antitumor agents
(basal cell carcinoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Antitumor agents
(bladder carcinoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Antitumor agents
(bronchi carcinoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Antitumor agents
(carcinoma, adenoid cystic carcinoma and others; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Bladder
Bladder
Bronchi
Bronchi
(carcinoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Antitumor agents
(carcinosarcoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Musculoskeletal diseases
(cartilage chondrosarcoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Uterus, neoplasm
Uterus, neoplasm
(cervix, inhibitors; cyclooxygenase-2 inhibitor and **matrix**

metalloproteinase inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(cervix; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Biliary tract
Biliary tract
(cholangioma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(cholangioma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Cartilage
Cartilage
(chondrosarcoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(chondrosarcoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(choroid plexus papilloma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Meninges
(choroid plexus, carcinoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Meninges
Meninges
(choroid plexus, papilloma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(colon carcinoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Intestine, neoplasm
Intestine, neoplasm
(colon, carcinoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
Carcinoid
Drug interactions
Hyperplasia
Radiotherapy
(cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(digestive tract; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Uterus, disease
(endometrium, hyperplasia; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Uterus

(endometrium, stroma, sarcoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Blood vessel, neoplasm
(endothelioma, hemangioendothelioma inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Spinal cord
(ependymal cell, ependymal neoplasia inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Neoplasm
(gastrinoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Neuroglia
Neuroglia
(glioblastoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Antitumor agents
(glioblastoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Pancreatic islet of Langerhans
Pancreatic islet of Langerhans
(glucagonoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Antitumor agents
(glucagonoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Antitumor agents
(head; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Blood vessel, neoplasm
(hemangioblastoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Blood vessel, neoplasm
Blood vessel, neoplasm
(hemangioma, inhibitors, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Antitumor agents
(hemangioma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Liver, disease
(hepatic adenomatosis; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Liver, neoplasm
Liver, neoplasm
(hepatoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Antitumor agents
(hepatoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)

IT Lung, neoplasm
(inhibitors, metastasis; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Adenoma
Lung, neoplasm
Lung, neoplasm
Pancreas, neoplasm
Pancreas, neoplasm
(inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Pancreatic islet of Langerhans
Pancreatic islet of Langerhans
(insulinoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(insulinoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(leiomyosarcoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(lentigo maligna melanoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(lung small-cell carcinoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(lung, metastasis; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
Antitumor agents
(lung; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(mammary gland; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(medulloblastoma, and medulloepithelioma inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Brain, neoplasm
Brain, neoplasm
(medulloblastoma, inhibitors, and medulloepithelioma inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(melanoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(meninges; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for

neoplasia treatment)
IT **Mesothelium**
Mesothelium
(mesothelioma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(mesothelioma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Carcinoma
Lung, neoplasm
(metastasis, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(metastasis; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT **Skin, neoplasm**
Skin, neoplasm
(mucoepidermoid **carcinoma**, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(mucoepidermoid carcinoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(multiple myeloma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(neck; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Capillary vessel
(neoplasia, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Digestive tract
Digestive tract
Gamete and Germ cell
Head
Head
Mammary gland
Mammary gland
Meninges
Meninges
Neck, anatomical
Neck, anatomical
Pituitary gland
(neoplasm, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Nerve, neoplasm
Nerve, neoplasm
(neuroblastoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(neuroblastoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for

neoplasia treatment)
IT Neuroglia
Neuroglia
(oligodendroglioma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(oligodendroglioma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Bone, neoplasm
Bone, neoplasm
(osteosarcoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(osteosarcoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
Antitumor agents
(pancreas; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(pinealoma inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Pineal gland
Pineal gland
(pinealoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Kidney, neoplasm
Kidney, neoplasm
(renal cell carcinoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(renal cell carcinoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Eye, neoplasm
Eye, neoplasm
(retinoblastoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(retinoblastoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(rhabdomyosarcoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(sarcoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Lung, neoplasm
Lung, neoplasm
(small-cell carcinoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination

therapy for neoplasia treatment)
IT Pancreatic islet of Langerhans
(somatostatinoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(squamous cell carcinoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Antitumor agents
(uvea melanoma; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT Eye, neoplasm
Eye, neoplasm
(uvea, melanoma, inhibitors; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT 39391-18-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(2; cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT 50-18-0, Cyclophosphamide 51-21-8, Fluorouracil 52-24-4, Thiotepa
53-86-1, Indomethacin 57-22-7, Vincristine 58-05-9, Leucovorin
76-43-7, Fluoxymesterone 128-13-2, Ursodeoxycholic acid 302-79-4,
Retinoic acid 471-34-1, Calcium carbonate, biological studies
865-21-4, Vinblastine 1464-42-2, Selenomethionine 3562-63-8, Megestrol
7782-49-2, Selenium, biological studies 10540-29-1, Tamoxifen
14769-73-4, Levamisole 15663-27-1, Cisplatin 15866-90-7 23214-92-8,
Doxorubicin 33069-62-4, Paclitaxel 33419-42-0, Etoposide 41575-94-4,
Carboplatin 51803-78-2 59973-80-7, Sulindac sulfone 65271-80-9,
Mitoxantrone 65277-42-1, Ketoconazole 65807-02-5, Goserelin
70052-12-9, Eflornithine 71486-22-1, Vinorelbine 80937-31-1
84449-90-1, Raloxifene 89778-26-7, Toremifene 93014-16-5 95058-81-4,
Gemcitabine 97682-44-5, Irinotecan 107868-30-4, Exemestane
112809-51-5, Letrozole 114977-28-5, Docetaxel 120511-73-1, Anastrozole
123653-11-2 123663-49-0 123948-87-8, Topotecan 154039-60-8
154361-50-9, Capecitabine 158205-05-1 158959-32-1 162011-90-7,
Rofecoxib 162054-19-5 169590-42-5, Celecoxib 170569-86-5
170569-87-6 170569-88-7 170630-40-7 177660-77-4 177660-95-6
178816-61-0 178816-94-9, [1,1':2',1''-Terphenyl]-4-sulfonamide
179382-91-3 179545-77-8 180200-68-4, JTE-522 181485-41-6
181695-72-7, Valdecoxib 181695-81-8 181696-33-3 187845-71-2
187845-80-3 189954-13-0 189954-16-3 191537-76-5 192329-42-3
197239-97-7 197239-99-9 197240-09-8 197240-14-5 197904-84-0
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226388-66-5 226389-91-9 226395-57-9 226395-66-0 226395-67-1
226395-93-3 226396-02-7 226396-03-8 226396-26-5 226703-01-1
227619-96-7 251972-30-2, SC-58236 279221-12-4 279221-13-5
279221-14-6 279221-15-7 279221-16-8 279221-17-9 279221-18-0
279221-19-1 279221-20-4 279221-21-5 279221-22-6 279221-23-7
279221-24-8 279221-25-9 279221-26-0 279221-27-1 279221-28-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitor and **matrix metalloproteinase** inhibitor in combination therapy for neoplasia treatment)
IT **141907-41-7, Matrix metalloproteinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cyclooxygenase-2 **inhibitor** and **matrix metalloproteinase inhibitor** in combination therapy

for neoplasia treatment)

L59 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1999:493072** HCAPLUS
DN **131:309512**
ED Entered STN: 10 Aug 1999
TI Differential expression of tissue inhibitors of **metalloproteinases** (TIMP-1, -2, -3, and -4) in normal and aberrant wound healing
AU Vaalamo, Maarit; Leivo, Tomi; Saarialho-Kere, Ulpu
CS Departments of Dermatology, Helsinki University Central Hospital and Central Military Hospital, and the Department of Anatomy, Institute of Biomedicine, University of Helsinki, Helsinki, Finland
SO Human Pathology (**1999**), 30(7), 795-802
CODEN: HPCQA4; ISSN: 0046-8177
PB W. B. Saunders Co.
DT Journal
LA English
CC 14-9 (Mammalian Pathological Biochemistry)
AB Wound healing is characterized by hemostasis, re-epithelialization, granulation tissue formation, and remodeling of the extracellular **matrix. Matrix metalloproteinases** and their specific inhibitors, TIMPs, contribute to these events. We investigated a total of 47 samples of normally healing wounds, chronic venous ulcers, ulcerative vasculitis, and suction blisters using immunohistochem. and in situ hybridization, to clarify the role of TIMPs in normal and aberrant wound repair. Expression of TIMP-1 and -3 mRNAs was found in proliferating keratinocytes in 3- to 5-day-old normally healing wounds, whereas no **epidermal** expression was detected in chronic ulcers. However, TIMP-3 protein was found in the proliferating **epidermis** in 20 of 24 samples representing both full-thickness acute and chronic wounds. TIMP-1 and TIMP-3 also were abundantly expressed by spindle-shaped, fibroblast-like, and plump, macrophage-like stromal cells, as well as by endothelial cells. In normally healing wounds, TIMP-2 protein localized under the migrating epithelial tip and to the stromal tissue under the eschar more frequently than in chronic ulcers. Occasional staining for TIMP-4 protein was detected in stromal cells of chronic ulcers near blood vessels. Our results indicate that TIMP-1 and TIMP-3 may be involved both in the regeneration of the **epidermis** by stabilizing the **basement membrane** zone and in the regulation of stromal remodeling and angiogenesis of the wound bed. Lack of TIMP-2 near the migrating epithelial wound edges might contribute to uncontrolled activity of **MMP**-2 in chronic ulcers. We conclude also that TIMPs are temporally and spatially tightly regulated and that the imbalance between **metalloproteinases** and TIMPs-1, -2, and -3 may lead to delayed wound healing.
ST **metalloproteinases** inhibitor TIMP **skin** wound healing
IT Gene, animal
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(TIMP-1; differential expression of tissue inhibitors of **metalloproteinases** (TIMP-1, -2, -3, and -4) in normal and aberrant wound healing in humans)
IT Gene, animal
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(TIMP-3; differential expression of tissue inhibitors of **metalloproteinases** (TIMP-1, -2, -3, and -4) in normal and aberrant wound healing in humans)
IT Gene, animal
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC

(Process)
(TIMP-4; differential expression of tissue inhibitors of **metalloproteinases** (TIMP-1, -2, -3, and -4) in normal and aberrant wound healing in humans)

IT Ulcer
(chronic venous; differential expression of tissue inhibitors of **metalloproteinases** (TIMP-1, -2, -3, and -4) in normal and aberrant wound healing in humans)

IT Angiogenesis
Basement membrane
Blister
Blood vessel
Cell proliferation
Extracellular **matrix**
Wound healing
(differential expression of tissue inhibitors of **metalloproteinases** (TIMP-1, -2, -3, and -4) in normal and aberrant wound healing in humans)

IT mRNA
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(differential expression of tissue inhibitors of **metalloproteinases** (TIMP-1, -2, -3, and -4) in normal and aberrant wound healing in humans)

IT Gene
(expression; differential expression of tissue inhibitors of **metalloproteinases** (TIMP-1, -2, -3, and -4) in normal and aberrant wound healing in humans)

IT **Skin**
(keratinocyte; differential expression of tissue inhibitors of **metalloproteinases** (TIMP-1, -2, -3, and -4) in normal and aberrant wound healing in humans)

IT Gene, animal
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(timp-2; differential expression of tissue inhibitors of **metalloproteinases** (TIMP-1, -2, -3, and -4) in normal and aberrant wound healing in humans)

IT Blood vessel, disease
(vasculitis, ulcerative; differential expression of tissue inhibitors of **metalloproteinases** (TIMP-1, -2, -3, and -4) in normal and aberrant wound healing in humans)

IT **124861-55-8**, TIMP-2 **140208-24-8**, TIMP-1
145809-21-8, TIMP-3 **186207-03-4**, TIMP-4
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(differential expression of tissue **inhibitors** of **metalloproteinases** (TIMP-1, -2, -3, and -4) in normal and aberrant wound healing in humans)

IT **141907-41-7**, **Matrix metalloproteinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(differential expression of tissue **inhibitors** of **metalloproteinases** (TIMP-1, -2, -3, and -4) in normal and aberrant wound healing in humans)

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L59 ANSWER 19 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1999:77667** HCAPLUS
DN **130:136300**
ED Entered STN: 05 Feb 1999
TI Methods for the preparation of **artificial** cellular tissue using **matrix metalloproteinase** inhibitors
IN Wolowacz, Richard; Wolowacz, Sorrel; Sheridan, Julie Marie
PA Smith & Nephew PLC, UK
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N005-06
ICS C07K014-81
CC 9-11 (Biochemical Methods)
Section cross-reference(s): 7, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9903979	A1	19990128	WO 1998-GB2147	19980717 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,

UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9884514 A1 19990210 AU 1998-84514 19980717 <--
PRAI GB 1997-14936 19970717 <--
WO 1998-GB2147 19980717 <--

AB There is disclosed the use of **matrix metalloproteinase** (**MMP**) inhibitors, e.g. collagenase, stromelysin, or gelatinase inhibitors in the production of tissue equivalent The inhibitors are used in particular to inhibit **MMPs** present in animal serum used in the production technique, thereby increasing collagen deposition. Tissue culture media and extracted animal serum containing a supplemented **MMP** inhibitor are also disclosed. Polylactic acid yarns seeded with fibroblasts of human fetal foreskin were cultured with media supplemented with doxycycline. Increased collagen content was observed in the test samples compared to control (lacking doxycycline).

ST **artificial** tissue prepn **matrix metalloproteinase** inhibitor; fibroblast tissue culture polylactic acid yarn doxycycline

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(N-1405, hydroxymate, inhibitor; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT Animal tissue culture
(animal serum in media for; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT Cartilage
(articular, **artificial**; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT Bone
Joint, anatomical
Ligament
Organ, animal
Skin
Tendon
Tendon
(**artificial**; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT Tetracyclines
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as nonselective inhibitor; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(braided tubular, as scaffold; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT **Epithelium**
Mesenchyme
(cells derived from; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT Blood vessel
(endothelium, cells derived from; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT **Skin**
(keratinocyte; **matrix metalloproteinase** inhibitors

in preparation of **artificial** cellular tissue)

IT Chondrocyte
Fibroblast
(**matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT Bone marrow
(mesenchymal stem cells of; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT Animal
(serum of, tissue culture media containing; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT Mesenchyme
(stem cell, of bone marrow; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT Mammal (Mammalia)
(supported cells of; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT Animal cell
(supported; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT Blood serum
(tissue culture media containing; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT **141907-41-7**, **Matrix metalloproteinase**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(activity of, in com. animal sera; **matrix metalloproteinase inhibitors** in preparation of **artificial** cellular tissue)

IT 60-54-8, Tetracycline **124861-55-8**, TIMP 2 **140208-24-8**, TIMP 1 142880-36-2, Galardin **145809-21-8**, TIMP 3 **186207-03-4**, Proteinase **inhibitor**, TIMP 4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as **inhibitor**; **matrix metalloproteinase inhibitors** in preparation of **artificial** cellular tissue)

IT 564-25-0, Doxycycline 808-26-4, Sancycline 10118-90-8, Minocycline
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as nonselective inhibitor; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT 60-54-8D, Tetracycline, chemical-modified
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as nonselective inhibitor; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT **86102-31-0**, Tissue **inhibitor** of **matrix metalloproteinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(as selective **inhibitor** of collagenase; **matrix metalloproteinase inhibitors** in preparation of **artificial** cellular tissue)

IT **141907-41-7D**, **Matrix metalloproteinase**, **inhibitors**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**matrix metalloproteinase inhibitors** in preparation of **artificial** cellular tissue)

IT 26009-03-0, Polyglycolic acid 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 34346-01-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(scaffold of three dimensional **matrix** of; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT 4464-01-1D, derivs.
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(selective collagenase inhibitor based on; **matrix metalloproteinase** inhibitors in preparation of **artificial** cellular tissue)

IT **9001-12-1**, Collagenase **9040-48-6**, Gelatinase **79955-99-0**, Stromelysin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(selective **inhibitor** of; **matrix metalloproteinase inhibitors** in preparation of **artificial** cellular tissue)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L59 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:683770 HCAPLUS
DN 130:79521
ED Entered STN: 29 Oct 1998
TI Proteinase requirements of **epidermal** growth factor-induced ovarian cancer cell invasion
AU Ellerbroek, Shawn M.; Hudson, Laurie G.; Stack, M. Sharon
CS Departments of Obstetrics & Gynecology and Cell & Molecular Biology, Northwestern University Medical School, Chicago, IL, USA
SO International Journal of Cancer (**1998**), 78(3), 331-337
CODEN: IJCNAW; ISSN: 0020-7136
PB Wiley-Liss, Inc.
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
AB Aberrant expression or activity of the **epidermal** growth factor (EGF) receptor family of tyrosine kinases has been associated with tumor progression and an invasive phenotype. In this study, the authors utilized 4 ovarian cancer cell lines, OVCA 432, DOV 13, OVEA6 and OVCA 429, to determine the effects of EGF on the regulation of proteolytic enzymes and their inhibitors, cellular migration and in vitro invasion. Induction of urinary-type plasminogen activator (u-PA) activity and tissue inhibitor of **matrix metalloproteinase** (TIMP)-1 was observed in all 4 cell lines. OVCA 432 cells showed strong PAI-1 induction; however, the other 3 lines displayed substantial baseline PAI-1 expression that was not induced by EGF. EGF-dependent stimulation of migration and induction of **matrix metalloproteinase** (**MMP**)-9 (gelatinase B) was observed in OVEA6 and OVCA 429 cells only. Upon EGF receptor activation, DOV 13, OVEA6 and OVCA 429 cells were induced to invade through an **artificial basement membrane** (Matrigel); however, no invasion was detected in OVCA 432 cells. Cell lines displaying induction of migration and **MMP**-9 (OVEA6 and OVCA 429) demonstrated robust EGF-induced invasion (5- to 20-fold), and cell invasion was substantially reduced in the presence of anti-catalytic

MMP-9 antibody. Addition of anti-catalytic u-PA antibody inhibited the modest (<2-fold) EGF-induced invasion in a cell line that did not express **MMP**-9 (DOV 13) and in OVEA6 cells that displayed the highest baseline u-PA activity. Together, the findings indicate that multiple proteinases are important in ovarian cell invasion and implicate EGF induction of **MMP**-9 and migration as key components of more aggressive ligand-induced invasion.

ST plasminogen activator **MMP9** EGF ovarian cancer invasion; proteinase ovarian cancer invasion metastasis

IT Ovary, neoplasm
(carcinoma; proteinase requirements of **epidermal** growth factor-induced human ovarian cancer cell invasion)

IT Ovary, neoplasm
Ovary, neoplasm
(metastasis; proteinase requirements of **epidermal** growth factor-induced human ovarian cancer cell invasion)

IT Cell migration
Ovary, neoplasm
(proteinase requirements of **epidermal** growth factor-induced human ovarian cancer cell invasion)

IT **Epidermal** growth factor receptors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(proteinase requirements of **epidermal** growth factor-induced human ovarian cancer cell invasion)

IT 62229-50-9, **Epidermal** growth factor
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(proteinase requirements of **epidermal** growth factor-induced human ovarian cancer cell invasion)

IT 9039-53-6, Plasminogen activator, urokinase-type 79079-06-4, EGF receptor kinase 140208-23-7, Proteinase inhibitor, PAI-1 **140208-24-8**, TIMP-1 **146480-36-6**, Gelatinase B
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(proteinase requirements of **epidermal** growth factor-induced human ovarian cancer cell invasion)

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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L59 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:434823 HCAPLUS
DN 129:177152
ED Entered STN: 15 Jul 1998
TI Collagen: a not so simple protein
AU Bailey, A. J.; Paul, R. G.
CS Collagen Research Group, University of Bristol, Bristol, BS18 7DY, UK
SO Journal of the Society of Leather Technologists and Chemists (**1998**), 82(3), 104-110
CODEN: JSLTBY; ISSN: 0144-0322
PB Society of Leather Technologists and Chemists
DT Journal; General Review
LA English
CC 45-0 (Industrial Organic Chemicals, Leather, Fats, and Waxes)
AB A review with 25 refs. Collagen is the major protein of animal bodies from simple sponges to Homo sapiens and exists in various forms from **skin**, tendon and bone to cornea and **basement membrane** of the capillaries. This biol. variation can now be accounted for on the basis of a whole family of genetically distinct collagens. Over the past two decades 19 different collagens have been identified, although the major types are the fibrous types I, II and III and the non-fibrous type IV of **basement membrane.** They all possess the basic triple helix based on multiple repeats of the simple tri-peptide Gly-X-Y, but this varies in length and forms different supramol. aggregates to achieve optimum function for particular tissues. The major function of collagen is to provide shape and mech. strength and the latter is achieved by intermol. crosslinking of the collagen mols. in the supramol. aggregate. The monomeric mols. in the aggregates are stabilized by two different pathways. Initially crosslinking occurs through an enzymic mechanism involving oxidation of specific lysine and hydroxylysine residues providing divalent crosslinking which subsequently matures to multivalent cross-links. As the rate of turnover decreases a non-enzymic pathway takes over, which is mediated through the adventitious accretion of glucose. Collagen therefore, unlike other proteins shows considerable changes with age which in turn affect its phys. properties. These changes must be taken into account when preparing collagen based products. All the amino acid side chains project radially from the rod-like triple helix and the quarter-staggered array of the mols. allows highly specific intermol. crosslinking either naturally, or **artificially** with bifunctional reagents. Reactions with basic or acid groups can therefore be carefully controlled and in some cases their location predicted. Synthetic cross-links bind the mols. closer together and increase intermol. interactions, thus increasing the shrinkage temperature and resistance to enzymic degradation The turnover of collagen is generally slow but in fact can vary from 2/3 days for periodontal ligament to several years for **skin** and tendon. Mature collagen fibers are highly resistant to enzymes and degradation is achieved by specific collagenase that can cleave the triple helix at one particular point. The shorter helical fragments can then unravel and denature to gelatin when other **metalloproteinases** (**MMPs**) degrade it to amino acids. A family of 14 **metalloproteinases** have been identified along with some specific tissue inhibitors (TIMPS). The sharp denaturation temperature of collagen attests to the almost crystalline character of the triple helix and the variation in shrinkage temperature between species is primarily due to the number of hydroxyproline based water hydrogen bridges. The presence of a hydroxyproline deficient thermally labile domain near the carboxy terminus of the mol. initiates the melting process allowing the triple helix to unzip along its length. Recent studies have demonstrated that collagen is not an inert structural material but

interacts with other mols. to control the development of collagenous tissues. Despite the ancient lineage of this ubiquitous protein, collagen is still revealing exciting new scientific features.
ST review collagen
IT Collagens, properties
RL: MSC (Miscellaneous); PRP (Properties)
(structure and properties of)
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L59 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1993:94038** HCAPLUS
DN **118:94038**
ED Entered STN: 19 Mar 1993
TI Protection of vascular **basement membrane** and microcirculation from elastase-induced damage with a fluorinated β-lactam derivative
AU Maillard, Jean Louis; Favreau, Catherine; Vergely, Isabelle; Reboud-Ravaux, Michele; Joyeau, Roger; Kobaiter, Randa; Wakselman, Michel
CS Inst. Jacques Monod, Univ. Paris VII, Paris, 75251, Fr.
SO Clinica Chimica Acta (**1992**), 213(1-3), 75-86
CODEN: CCATAR; ISSN: 0009-8981
DT Journal
LA English
CC 1-8 (Pharmacology)
AB N-(2-Chloromethylphenyl) 3,3-difluoroazetidin-2-one (AA 231-1), a specific suicide-type inhibitor of elastase which is known to suppress the lysis of chromogenic oligopeptides, elastin and elastic fibers, is effective also in preventing the degradation of the vascular **basement membrane**. The degradation of porcine glomerular **basement membrane** by purified human leukocyte elastase (HLE), was reduced in proportion of inhibitor dose (8.3 μM for 50% inhibition). It is noteworthy that there was no reduction of the inhibitory effect when the addition of AA 231-1 was delayed for 1 h after the addition of the enzyme to the substrate. In the guinea pig, reduction of the **dermal**

microhemorrhage due to HLE was related to the dose of inhibitor and to its preincubation time with HLE before intradermal injection. The inflammatory hemorrhage associated with the Arthus **skin** reaction was moderately depressed by AA 231-1 in situ. A part of the vascular permeability induced by HLE also responded to the inhibitor. In spite of the tissular diffusion and the time-dependence parameters which restrict responsiveness of elastase to AA 231-1 in vivo this biochem. compound should be helpful in the study and possibly the cure of vascular injury related to elastase.

ST elastase inhibitor blood vessel injury

IT Blood vessel, toxic chemical and physical damage
(elastase damage to, in **basement membrane**, fluorinated β-lactam derivative AA 231-1 inhibition of)

IT Neutrophil
(vascular **basement membrane** damage by elastase from, fluorinated β-lactam derivative AA 231-1 inhibition of)

IT **Basement membrane**
(vascular, elastase damage to, fluorinated β-lactam derivative AA 231-1 inhibition of)

IT **9004-06-2**, Elastase
RL: BIOL (Biological study)
(vascular **basement membrane** damage by, from polymorphonuclear neutrophil leukocytes, fluorinated β-lactam derivative AA 231-1 **inhibition** of)

IT 131230-67-6, AA 231-1
RL: BIOL (Biological study)
(vascular **basement membrane** protection from elastase-induced damage by)

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>>> THE DISPLAY LAYOUT HAS BEEN CHANGED TO ACCOMODATE THE NEW FORMAT GERMAN PATENT APPLICATION AND PUBLICATION NUMBERS. SEE ALSO:

http://www.stn-international.de/archive/stnews/news0104.pdf <<<

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L81 ANSWER 1 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2004-172312 [17] WPIX
DNC C2004-068652
TI **Matrix metalloprotease** inhibitor useful as cosmetics such as ointment, cream, milky lotion, lotion, pack and bath agent, for preventing aging of skin, wrinkles and sag, consists of catechin, procyanidins and/or mangosteens.
DC B02 D21 E13
PA (SHIS) **SHISEIDO CO LTD**
CYC 1
PI JP 2003252745 A 20030910 (200417)* 10 A61K007-48 <--
ADT JP 2003252745 A JP 2002-52878 20020228
PRAI JP 2002-52878 20020228
IC ICM **A61K007-48**
ICS **A61K007-00**
AB JP2003252745 A UPAB: 20040310
NOVELTY - A **matrix metalloprotease** inhibitor consists of catechin, procyanidins and/or mangosteens.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) an elastin degradation inhibitor;
(2) a laminin degradation inhibitor;
(3) a **basement membrane** degradation inhibitor;
(4) a proteoglycan degradation inhibitor;
(5) a collagen degradation inhibitor; and
(6) cosmetics which contain **matrix metalloprotease** inhibitor.
ACTIVITY - Dermatological.
MECHANISM OF ACTION - **Matrix metalloprotease** inhibitor.
USE - As ointment, cream, milky lotion, lotion, pack, bath agent, etc for preventing aging of skin, wrinkles and sag.
ADVANTAGE - The **matrix metalloprotease** (**MMPs**) has excellent **MMP1**, **MMP3** and **MMP9** inhibitory activity. The cosmetics effectively maintain the state of youthful skin by preventing aging, wrinkles and sag.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B06-A01; B14-D03; B14-L06; **B14-N17**; **D08-B09A**; E06-A01
TECH UPTX: 20040310
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The **matrix metalloprotease** belongs to gelatinase group, stromelysin group and/or collagenase group.
ABEX UPTX: 20040310
EXAMPLE - Fruit skin mangosteen was extracted with methanol to obtain alpha-mangosteen having **matrix metalloprotease** inhibiting activity. A cream was formulated by compounding (in mass%) stearic acid (5), stearyl alcohol (4), isopropyl myristate (18), glycerol monostearin acid ester (3), propylene glycol (10), alpha-mangostin (0.01), caustic potash (0.2), sodium hydrogensulfite (0.01), preservative (sufficient amount), fragrance (sufficient amount) and ion exchange water (remaining quantity).

L81 ANSWER 2 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-897817 [82] WPIX
CR 1996-300644 [30]; 2002-462907 [49]; 2002-706411 [76]; 2003-045548 [04]
DNN N2003-716547 DNC C2003-254983
TI New polynucleotide encoding a tissue inhibitor of

metalloproteinase designated TIMP-4 is useful to treat **metalloproteinase** associated disease including restenosis and collagenase-associated disease.

DC B04 D16 S03
IN GREENE, J M; ROSEN, C A
PA (GREE-I) GREENE J M; (ROSE-I) ROSEN C A
CYC 1
PI US 2003157687 A1 20030821 (200382)* 61 C12Q001-68
ADT US 2003157687 A1 CIP of WO 1994-US14498 19941213, Cont of US 1995-463261 19950605, CIP of US 1999-387525 19990901, Provisional US 2000-217419P 20000711, Provisional US 2000-220829P 20000726, Div ex US 2001-901904 20010711, US 2003-366445 20030214
FDT US 2003157687 A1 Cont of US 6448042, Div ex US 6544761
PRAI US 2003-366445 20030214; WO 1994-US14498 19941213;
US 1995-463261 19950605; US 1999-387525 19990901;
US 2000-217419P 20000711; US 2000-220829P 20000726;
US 2001-901904 20010711
IC ICM C12Q001-68
ICS A61K038-46; A61K048-00; C07H021-04; C12N009-64; G01N033-53
AB US2003157687 A UPAB: 20031223
NOVELTY - An isolated polynucleotide encoding a tissue inhibitor of **metalloproteinase** designated TIMP-4 is new.

DETAILED DESCRIPTION - A new isolated polynucleotide (N1) comprises:

(a) a polynucleotide encoding a 224 amino acid sequence fully defined in the specification (sequence I);

(b) a polynucleotide sequence which hybridizes to and is at least 70% identical to (a); or

(c) a fragment of (a) or (b).

INDEPENDENT CLAIMS are also included for

(1) an isolated polynucleotide comprising:

(a) a polynucleotide encoding a mature polypeptide encoded by the DNA contained in American type culture collection (ATCC) deposit number 75946;

(b) a polynucleotide which encodes a polypeptide expressed by the DNA contained in ATCC deposit number 75946;

(c) a polynucleotide capable of hybridizing to and at least 70% identical to the polynucleotide of (a) or (b); or

(d) a fragment of (a), (b) or (c);

(2) a vector comprising N1 DNA;

(3) a host cell genetically engineered with the above vector;

(4) producing a polypeptide comprises expressing from the above host cell the polypeptide encoded by the DNA;

(5) producing cells capable of expressing a polypeptide comprising transforming or transfecting cells with the above vector;

(6) a polypeptide comprising:

(a) a polypeptide (P1) having sequence I or its fragment, analogue or derivative;

(b) a polypeptide comprising amino acids 1-195 of sequence I; or

(c) a polypeptide encoded by the cDNA contained in ATCC deposit number 75946 or its fragment, analogue or derivative;

(7) a P1 agonist;

(8) a P1 antagonist;

(9) treating a patient needing TIMP-4, comprising administering P1 or the P1 agonist;

(10) treating a patient needing TIMP-4 inhibition comprising administering the P1 antagonist;

(11) identifying P1 agonists of antagonists comprises combining an **matrix metalloproteinase** (**MMP**), human TIMP-4, a candidate compound and a reaction mixture containing labeled substrate capable of degradation by **MMP**, and determining ability of the candidate compound to block or enhance degradation of the substrate by **MMP** by measuring released label;

(12) diagnosing a disease or disease susceptibility, comprising determining a mutation in the human TIMP-4 nucleic acid sequence; and

(13) treating restenosis, comprises administering a nucleic acid encoding a TIMP-4 polypeptide having residues -29 to 195, -28 to 195 or 1 to 195 of sequence I or a fragment of sequence I which retains protease activity

ACTIVITY - Vasotropic; Antiasthmatic; Dermatological; Nephrotropic; Antirheumatic; Antiarthritic; Antipsoriatic; Osteopathic; Cytostatic; Vulnerary; Antithyroid; Antiulcer; Neuroprotective; Antibacterial; Immunosuppressive. Adenoviral construct expressing rat TIMP-4 or null vector was administered to 12 rats directly after carotid artery balloon injury. After 14 days there was a significant 74% reduction in neointimal area in Ad-TIMP-4 infected vessels compared with Ad-null infection (1.04 plus or minus 0.32 mm2 compared to 5.03 plus or minus 1.66 mm2, p= 0.00018). No difference was seen in medial area. The ratio of neointima to media showed a significant difference between Ad-TIM-4 and Ad-Null infected vessels (0.18 plus or minus 0.05 versus 0.80 plus or minus 0.16, p= 0.01). These results showed that adenovirus-mediated gene transfer of rat TIMP-4 to the rat carotid artery immediately after injury causes a significant decrease in neointima development.

MECHANISM OF ACTION - **Metalloproteinase** inhibitor.

USE - The invention is used to treat restenosis (claimed). Other disease which may be treated include arthritic diseases such as rheumatoid and osteoarthritis, soft tissue rheumatism, polychondritis and tendonitis, bone resorption diseases such as osteoporosis, Paget's disease, hyperthyroidism and cholesteatoma, the enhanced collagen destruction that occurs with diabetes, the recessive classes of dystrophic epidermolysis bullosa, periodontal disease, alveolitis and related consequences of gingival production of collagenase, corneal ulceration, ulceration of the skin and gastro-intestinal tract and abnormal wound healing, post-operative conditions in which collagenase levels are raised, cancer by blocking the destruction of tissue **basement membranes** leading to cancer metastases, demyelinating disease of the central and peripheral nervous systems, asthma, glomerulosclerosis, septic shock and infection, and psoriasis.

Dwg.0/10

FS CPI EPI
FA AB
MC CPI: B04-C01G; B04-E03F; B04-E08; B04-F0100E; B04-F11; B04-L05C; B04-M01; B04-N04A0E; B11-C08E; B11-C08F; B12-K04A; B12-K04E; B14-C06; B14-C09A; B14-C09B; B14-D07C; B14-E08; B14-F01G; B14-H01; B14-K01A; B14-L01; B14-L06; B14-N01; B14-N10; B14-N11; **B14-N17**; B14-S01; B14-S03A; B14-S06; D05-A02C; D05-H09; D05-H12A; D05-H12E; D05-H14; D05-H17A6; D05-H18
EPI: S03-E14H
ABEX UPTX: 20031223

ADMINISTRATION - The TIMP-4 nucleic acid sequence is preferably delivered in a viral vector delivery vehicle, particularly a vehicle from adenovirus. No further details provided.

EXAMPLE - No suitable example provided.

L81 ANSWER 3 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-819640 [77] WPIX
DNC C2003-230255
TI **Matrix metalloprotease** activity inhibitor for use in cosmetics, comprising solvent extract of plant selected from coconut, Blumea balsamifera, Guarana, Smilax officinalis or Smilax aspera.
DC B04 D21
PA (SHIS) **SHISEIDO CO LTD**
CYC 1
PI JP 2003201229 A 20030718 (200377)* 16 A61K007-48 <--
ADT JP 2003201229 A JP 2002-207951 20020717
PRAI JP 2001-325605 20011023
IC ICM **A61K007-48**

ICS **A61K007-00**; A61K035-78; A61P003-00; **A61P017-00**; A61P043-00

AB JP2003201229 A UPAB: 20031128
NOVELTY - A **matrix metalloprotease (MMPs)** activity inhibitor (I) contains solvent extract of plant selected from coconut (Cocos nucifera), Blumea balsamifera, Illicium verum, Juniperus brasiliensis, Salix alba, Guarana, Smilax officinalis, Smilax aristolochiaefolia or Smilax aspera.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for cosmetics for anti-aging, comprising (I).
ACTIVITY - Dermatological.
MECHANISM OF ACTION - **Matrix metalloprotease** inhibitor.
Cocos nucifera plant extract was dissolved in 2 mass% of dimethyl sulfoxide to obtain a sample solution. The sample solution was diluted with buffer containing 0.4 M sodium chloride and 10 mM of calcium chloride. Enzyme belonging to stromelysin derived from human cell was used as **matrix metalloprotease.** Substance containing 50 micro l of sample solution, 100 micro l of enzyme solution containing 0.4 unit/ml of enzyme and 50 micro l of fluorescent labeling substrate, was incubated at 42 deg. C for 2 - 4 hours. Ethanol solution was added and unreacted substrate was centrifuged. The fluorescence intensity of decomposed substance in the supernatant liquid was measured. The decomposition ratio of substrate was calculated to measure **MMPs** activity inhibitory effect. The plant extract sample solution was found to have **MMPs** activity inhibitory effect of 49%.
USE - For use in cosmetics such as cream, milky lotion, makeup cosmetics, hair cosmetics, and bathing agent, and for use in pharmaceuticals.
ADVANTAGE - The cosmetic improves and prevents skin aging such as wrinkles, and maintains youthful skin without wrinkle or sag.
Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B04-A08; B04-A10; B04-L01; B14-D07C; B14-L06; **B14-N17**; **B14-R01**; B14-R02; D08-B

TECH UPTX: 20031128
TECHNOLOGY FOCUS - BIOLOGY - Preferred Materials: (I) Further contains enzymes belonging to gellatinase group, stromelysin group and collagenase group. (I) Is an elastin decomposition inhibitor, laminin decomposition inhibitor, **basement-membrane** decomposition inhibitor, proteoglycan decomposition inhibitor or collagen decomposition inhibitor.

ABEX UPTX: 20031128
EXAMPLE - Cocos nucifera plant was immersed with methanol for 1 week at room temperature and extracted. The extract was concentrated to obtain plant extract. Aqueous phase was prepared by dissolving (in mass%) propylene glycol (10), coconut extract (0.01), and caustic potash (0.2) in ion exchange water and heating at 70 degrees C. Oil-phase was prepared by melting stearic acid (5), stearyl alcohol (4), isopropyl myristate (18), glycerol monostearic acid ester (3), sodium hydrogen sulfite (0.01), suitable quantity of preservative and fragrance at 70 degrees C. Oil-phase was added to the aqueous phase, emulsified and cooled to 30 degrees C to obtain cream. The obtained cream was found to have aging prevention effect.

L81 ANSWER 4 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2003-819638 [77] WPIX

DNC C2003-230253

TI **Matrix metalloprotease** activity inhibitor for use in skin external preparation such as cosmetics, contains solvent extract of plant chosen from Schima wallichii, Desmodium triquetrum, Equisetum debile or Bombax ceiba.

DC B04 D16 D21

PA (SHIS) **SHISEIDO CO LTD**
CYC 1
PI JP 2003201212 A 20030718 (200377)* 16 A61K007-00 <--
ADT JP 2003201212 A JP 2002-263190 20020909
PRAI JP 2001-325607 20011023
IC ICM **A61K007-00**
ICS **A61K007-48**; A61K035-78; **A61P017-16**; A61P043-00
AB JP2003201212 A UPAB: 20031128
NOVELTY - A **matrix metalloprotease** (**MMPs**) activity inhibitor contains solvent extract of the plant chosen from Schima wallichii, Taxillus Kaempferi, Cinnamomum iners, Desmodium triquetrum, Artocarpus elasticus, Equisetum debile or Bombax ceiba.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for skin external preparation which contains the solvent extract of the plant chosen from Schima wallichii, Taxillus Kaempferi, Cinnamomum iners, Desmodium triquetrum, Artocarpus elasticus, Equisetum debile or Bombax ceiba.

ACTIVITY - Dermatological.

MECHANISM OF ACTION - **Matrix metalloprotease** inhibitor. Schima noronhae plant extract was dissolved in 2 mass % of dimethyl sulfoxide to obtain a sample solution. The sample solution was diluted with buffer containing 0.4M sodium chloride and 10 mM of calcium chloride. Enzyme belongs to stromelysin derived from human cell was used as **matrix metalloprotease.** 50 micro liter of sample solution, 100 micro liter of enzyme solution containing 0.4 unit/ml of enzyme and 50 micro liter of fluorescent labeling substrate. The above substance was incubated at 42 deg. C for 2-4 hours. Ethanol solution was added and unreacted substrate was centrifuged after the enzyme reaction is completed. The fluorescence intensity of decomposed substance in the supernatant liquid was measured. The decomposition ratio of substrate was calculated. The plant extract sample solution was found to have **MMPs** activity inhibitory effect of 33%.

USE - For use in skin external preparation such as cosmetics e.g. cream, milky lotion, makeup cosmetics, hair cosmetics, bathing agent, etc., and for use in pharmaceuticals. The skin external preparation improves and prevents skin ageing such as wrinkles. The skin external preparation maintains the youthful skin without wrinkle or sag.

Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-A10; **B14-N17**; **B14-R01**; D05-A02; **D08-B09A1**; **D08-B09A3**
TECH UPTX: 20031128
TECHNOLOGY FOCUS - BIOLOGY - Preferred Materials: The **matrix metalloprotease** activity inhibitor further contains enzymes belongs to gellatinase group, stromelysin group and collagenase group. The **matrix metalloprotease** activity inhibitor is an elastin decomposition inhibitor, laminin decomposition inhibitor and **basement-membrane** decomposition inhibitor, proteoglycan decomposition inhibitor and collagen decomposition inhibitor.
ABEX UPTX: 20031128
EXAMPLE - Schima noronhae plant was immersed with methanol for 1 week at room temperature and extracted. The extract was concentrated to obtain plant extract. Aqueous phase was prepared by dissolving (in mass %) propylene glycol (10), Schima noronhae extract (0.01), and caustic potash (0.2) in ion exchange water and heating at 70 degrees C. Oil-phase was prepared by melting stearic acid (5), stearyl alcohol (4), isopropyl myristate (18), glycerol monostearic acid ester (3), sodium hydrogen sulfite (0.01), suitable quantity of preservative and fragrance at 70 degrees C. Oil-phase was added to the aqueous phase, emulsified and cooled to 30 degrees C to obtain cream. The obtained cream was found to have ageing prevention effect.

L81 ANSWER 5 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-818769 [77] WPIX
DNC C2003-229507
TI Skin external preparation for anti-ageing composition, comprises plant extract(s) chosen from Persea gratissima, Picea abies, Rubus fructicosus, Malus sylvestris, Cinchona succirubra and Theobroma cacao.
DC B04 D21
PA (SHIS) **SHISEIDO CO LTD**
CYC 1
PI JP 2003160433 A 20030603 (200377)* 9 A61K007-00 <--
ADT JP 2003160433 A JP 2001-360780 20011127
PRAI JP 2001-360780 20011127
IC ICM **A61K007-00**
ICS **A61K007-48**; A61K035-78; **A61P017-16**; A61P043-00
AB JP2003160433 A UPAB: 20031128
NOVELTY - A skin external preparation comprises plant extract(s) chosen from Persea gratissima, Picea abies, Rubus fructicosus, Malus sylvestris, Cinchona succirubra and Theobroma cacao, as active ingredient.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(1) **matrix metalloprotease (MMP)** inhibitor belonging to gelatinase, stromelysin or collaginase group, comprising above plant extract;
(2) elastin decomposition inhibitor comprising above plant extract;
(3) laminin decomposition inhibitor comprising above plant extract;
(4) **basement-membrane** decomposition inhibitor comprising above plant extract;
(5) proteoglycan decomposition inhibitor comprising above plant extract;
(6) collagen decomposition inhibitor comprising above plant extract; and
(7) cosmetics comprising above plant extract.
USE - For **matrix metalloprotease** inhibitor, elastin decomposition inhibitor, laminin decomposition inhibitor, **basement-membrane** decomposition inhibitor, proteoglycan decomposition inhibitor, collagen decomposition inhibitor and cosmetics (all claimed) preferably anti-ageing composition, hair cosmetics and bathing agent.
ADVANTAGE - The skin external preparation has excellent **MMP9**, **MMP3** and **MMP1** activity inhibitory effect, prevents decomposition of skin extracellular **matrix** component, and provides youthful skin by preventing ageing of skin. The skin external preparation prevents formation of wrinkles or sag, and is elastic.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-A08; B04-A09; B04-A10; B14-D03; **B14-R01**; **D08-B09A3**
ABEX UPTX: 20031128
EXAMPLE - 50 g of each of Picea abies and Malus sylvestris plant extract was immersed in ethanol for 1 week at room temperature. The extract was concentrated and dissolved in dimethyl sulfoxide. The solution was diluted and its concentration was adjusted. Picea abies extract of concentration 0.0005 was evaluated for **MMP9** activity inhibitory effect, and the inhibitor percentage was found to be 24, and Malus sylvestris of concentration 0.001 was evaluated for **MMP9** activity inhibitory effect, and the inhibitor percentage was found to be 38. Stearic acid (in mass%) (2), stearyl alcohol hydrogenated lanolin (2), squalane (5), 2-octyl dodecylalcohol (6), polyoxyethylene cetyl alcohol ether (3), glycerol monostearic acid ester (2), propylene glycol (5), extract of Picea abies (0.05), sodium hydrogen sulfite (0.03), ethyl paraben (0.3), suitable amount of fragrance and ion exchange water were taken. Propylene glycol was added to ion exchange water and heated to 70 degrees C to form

a water phase. The other components were mixed and melted at 70degreesC to form an oil phase. The oil phase was added to the water phase, and preliminary emulsification was carried out. The emulsion was cooled to 30 degrees C, and a cream was prepared.

L81 ANSWER 6 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-622126 [59] WPIX
DNC C2003-170359
TI Inhibitor of **matrix metalloprotease** of the gelatinase, stromelysin or collagenase groups contains plant material or extract of e.g. rhubarb, sage, avocado, tamarind, Luehea genus plant, for anti-ageing cosmetics for skin and hair.
DC B04 D21
PA (SHIS) **SHISEIDO CO LTD**
CYC 1
PI JP 2003201214 A 20030718 (200359)* 20 A61K007-00 <--
ADT JP 2003201214 A JP 2002-207952 20020717
PRAI JP 2001-325606 20011023
IC ICM **A61K007-00**
ICS A61K035-78; A61P043-00
AB JP2003201214 A UPAB: 20030915
NOVELTY - An inhibitor of a gelatinase group and/or stromelysin group **matrix metalloprotease** (**MMP**) contains one or more of e.g.Woodfordia floribunda Salisb., Persea americana Mill., Rheum sp., Cassia angustifolia Vahl, Garcinia mangostana L., Cinnamomum cassia Bl., Tamarindus indica L., Bergenia ciliata (Haw.) Sternb., L. grandiflora Mart. et Zucc., L. ochrophylla Mart. or their solvent extracts

DETAILED DESCRIPTION - An inhibitor of a gelatinase group and/or stromelysin group **matrix metalloprotease** (**MMP**) contains one or more plant chosen from Woodfordia floribunda Salisb., Persea americana Mill., Rheum sp., Cassia angustifolia Vahl, Garcinia mangostana L., Cinnamomum cassia Bl., Tamarindus indica L., Bergenia ciliata (Haw.) Sternb., Luehea divaricata Mart. et Zucc., Luehea grandiflora Mart. et Zucc., Luehea ochrophylla Mart., Luehea paniculata Mart. et Zucc., Luehea rufescens A. St. Hil., Arctium lappa L., Arctium minus, Anemopaegma arvense (Vell.), Anemopaegma glaucum Mrt. ex DC., Erythroxylum vaccinifolium Mart., Margaritaria nobilis L. f., and Pouteria obtusifolia Baehni, or their solvent extracts.

An INDEPENDENT CLAIM is made for an inhibitor of a collagenase **MMP**, containing one or more of the plants or their solvent extracts.

USE - The inhibitor is an anti-ageing agent used to prevent or improve skin ageing by inhibiting decomposition of skin extra-cellular-**matrix** components such as elastin, laminin, proteoglycan, **basement membrane** component or collagen, including wrinkles and sagging, for use in cosmetics, hair cosmetics.

ADVANTAGE - The inhibitor is highly effective when in contact with the skin. It does not damage skin fiber.

Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-A08; B04-A10; B04-D02; B11-A; B12-M02; B12-M03; B14-D03; B14-L06; **B14-R01**; D08-B; **D08-B09A3**; D08-B10
TECH UPTX: 20030915
TECHNOLOGY FOCUS - BIOLOGY - Preferred inhibitor: the inhibitor inhibits the decomposition of elastin, laminin, **basement-membrane**, proteoglycan or collagen.
ABEX UPTX: 20030915
EXAMPLE - An extract of Woodfordia floribunda was made from the leaves and flower of the plant (200 g) by immersing in methanol (550 ml) for one week at room temperature, then concentrating, giving extracted material (33.25 g). The extracted material was dissolved at 2 mass % in dimethyl sulfoxide (DMSO), and diluting with 0.1M TRIS of pH 7.4 (containing 0.4M NaCl and 10

mM CaCl2). This solution, at concentration 0.0005 weight %, inhibited **MMP**-9 (gelatinase group) by 25% and at 0.001 weight % inhibited **MMP3** (stromelysin) by 10% and **MMP1** (collagenase) by 20%.
A cream was prepared from (mass %) stearic acid (5.0); stearyl alcohol (4.0); isopropyl myristate 1(8.0); glyceryl monostearate (3.0); propylene glycol (10.0); Woodfordia floribunda extract (0.01) (50 % 1,3 butylene glycol extract, 2.01 % concentration); caustic potash (0.2); sodium hydrogen sulfite (0.01); preservative (suitable quantity); fragrance (suitable quantity); water (remainder) by forming an aqueous phase by dissolving the propylene glycol, Woodfordia floribunda extract and caustic potash in the water; making an oil phase by melting the other ingredients; adding the oil phase gradually to the aqueous phase at 70 degrees C, mixing and cooling. This cream had an excellent **MMP** inhibitory effect (no further details).

L81 ANSWER 7 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-572596 [54] WPIX
DNC C2003-154942
TI New dithiazole compounds are **matrix metalloproteinase** inhibitors, useful for preventing e.g. skin aging, wrinkles, rheumatic arthritis and osteoarthritis.
DC B02 B03 D21
IN HIRUMA, T; **INOMATA, S**; KOBAYASHI, K
PA (SHIS) **SHISEIDO CO LTD**
CYC 28
PI JP 2003064065 A 20030305 (200354)* 38 C07D285-01
WO 2003020711 A1 20030313 (200354) JA C07D285-01
RW: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR
W: CN KR US
EP 1422224 A1 20040526 (200435) EN C07D285-01
R: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LU MC NL PT SE SK TR
ADT JP 2003064065 A JP 2001-258066 20010828; WO 2003020711 A1 WO 2002-JP8649 20020828; EP 1422224 A1 EP 2002-772819 20020828, WO 2002-JP8649 20020828
FDT EP 1422224 A1 Based on WO 2003020711
PRAI JP 2001-258066 20010828
IC ICM C07D285-01
ICS A61K007-00; A61K007-48; A61K031-41; A61K031-4439; A61K031-4709; A61K031-5377; A61P001-04; A61P003-00; A61P017-00; A61P019-02; A61P035-00; A61P043-00; C07D417-12; C07D417-14
AB JP2003064065 A UPAB: 20030821
NOVELTY - Dithiazole compounds (I) are new.
DETAILED DESCRIPTION - Dithiazole compounds of formula (I) and their salts are new.
R1 = H, alkyl, alkenyl, aryl, arylalkyl, heteroaryl alkyl, heteroarylthio alkyl, OH, alkoxy alkyl or Het-alkyl;
Het = heterocyclic ring containing 5- or at least 16-membered N atoms coupled with alkyl group;
R2 = H, alkyl, aryl, arylalkyl, heteroaryl, heteroaryl alkyl, OH, alkoxy, H(CxH2xO)m-, arylalkoxy, hydroxyalkyl, acyloxyalkyl, alkoxyalkyl, alkoxy(aryl or heteroaryl)alkyl, alkylthio, alkylsulfinyl, alkylsulfonyl alkyl, alkylamino, alkylaminoalkyl, acylaminoalkyl, amino, acylamino or Het-alkyl;
x = 1-3;
m = 2-5;
R3 = a group of formula (i)-(iii);
A = alkyl, alkoxy, aryl, aryloxy, heteroaryl, aryl-Z1-amino aryl or aryl amino-Z1-aryl;
R4 = H, alkyl, aryl, arylalkyl, heteroaryl, heteroaryl alkyl, hydroxyalkyl, acyloxy alkyl, alkoxy alkyl, alkylthio, alkylsulfinyl, alkylsulfonyl alkyl, alkylamino, alkylaminoalkyl, acylamino alkyl, group A-Y-N(R4)-CR1R2-CONH- which may of formula (iv);

R5-R7 = H, alkyl, alkenyl, aryl, heteroaryl, arylalkyl, heteroaryl alkyl, halogen atom, amino, alkyl amino, aminoaryl aminoheteroaryl, (aryl or heteroaryl) alkylamino, acylamino, (alkyl, aryl or heteroaryl)-Z2-amino, OH, alkoxy, H(CxH2xO)m-, alkenyloxy, aryloxy, heteroaryl oxy, acyl, acyloxy, alkoxy (aryl or heteroaryl), (alkyl, aryl or heteroaryl)-Z3-oxy, mercapto, alkylthio, arylthio, heteroarylthio, acylthio, alkylthio (aryl or heteroaryl) or (alkyl, aryl or heteroaryl)-Z4-thio;

Y, Z1-Z4 = -SO2- or -CO-;

n = 0-1,

R8 = H or alkyl;

R9 = side chain of alpha -amino acid;

R10 = H, alkyl, alkenyl or arylalkyl and

Ring B = 1,2,3,4-tetrahydro isoquinoline, piperidine, oxazolidine, thiazolidine, pyrrolidine, morpholine, piperazine or thiomorpholine;

provided that when n = 1, compound (I) is of formula (I').

INDEPENDENT CLAIMS are also included for:

(1) a **matrix metalloproteinase** activation inhibitor which contains dithiazole compound or its salt as active ingredient;

(2) cosmetic composition which contains a dithiazole compound or its salt;

(3) pharmaceutical composition which contains a dithiazole compound or its salt; and

(4) external preparation for skin which contains a dithiazole compound or its salt.

ACTIVITY - Antirheumatic; Antiarthritic; Osteopathic; Antiinflammatory; Neuroprotective; Cytostatic; Antiulcer.

No biological data given.

MECHANISM OF ACTION - **Matrix-Metalloproteinase** -Inhibitor.

The ability of the 2-(4-((4-fluorobenzyl)oxy)phenyl)-3-methyl-N-(3-thioxo-3H-1,2,4-dithiazole-5-yl)butanamide (Ia) to inhibit **matrix metalloproteinase** (**MMPs**) was evaluated using **MMP** -9 (crude enzyme liquid derived from the mouse skin). The decrease in bandwidth corresponding to **MMP**-9 was evaluated by gelatin zymography method. Result showed that a sample solution containing (Ia) had significant **MMP** inhibitory effect when compared to the control.

USE - As pharmaceuticals and cosmetics (claimed) such as creams, milky lotions etc. for preventing skin aging, wrinkles, sag, rheumatic arthritis, osteoarthritis, osteoporosis, periodontal disease, multiple sclerosis, tumor metastasis and tissue ulcer formation.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B07-F03; B14-C09; B14-D03; B14-H01; B14-N01; B14-N06B; B14-N17; B14-R01; B14-S01; D08-B09A1

ABEX UPTX: 20030821

ADMINISTRATION - Administration of (I) is 0.1-500 mg/kg orally or parenterally.

EXAMPLE - 2-(p-hydroxyphenyl) isovaleric acid (3 g) was dissolved in methanol (30 ml). To the solution, sulfuric acid (0.82 ml) was added and the solvent was distilled for 13 hours under reflux conditions. The residue was neutralized by adding sodium hydrogen carbonate and extracted with ethyl acetate. The organic phase was washed in saturated salt solution and the solvent was distilled after drying using magnesium sulfate. The obtained residue was dissolved in acetone (31 ml). To the solution, potassium carbonate (4.27 g) and 4-fluorobenzyl chloride (3.69 ml) were added. The organic phase was washed with saturated salt solution and distilled after drying using magnesium sulfate. The obtained residue was dissolved in liquid mixture containing methanol (40 ml), tetrahydrofuran (40 ml) and potassium hydroxide (40 ml). The solvent was

refluxed for 64 hours and extracted by adding ethyl acetate and hydrochloric acid. The organic phase was washed with saturated salt solution and distilled after drying using magnesium sulfate. The obtained residue was recrystallized to obtain 2-(4-((4-fluoro benzyl)oxy)phenyl)-3-methyl butanoic acid. 2-(4-((4-fluoro benzyl)oxy)phenyl)-3-methyl butanoic acid (1 g) was dissolved in tetrahydrofuran (11 ml). To the solution 1,1'-carbonyl-diimidazole (0.644 g) was added. To the mixture, solution containing sodium hydroxide (0.132 g) suspended in tetrahydrofuran (11 ml) and 3-amino-1,2,4-dithiazole-5-thione (0.497 g) was added. To the solution saturated ammonium chloride was added and extracted with ethyl acetate. The organic phase was dried using saturated sodium hydrogen carbonate solution and saturated salt solution. The obtained residue was attached to silica gel column chromatography to obtain 2-(4-((4-fluorobenzyl)oxy)phenyl)-3-methyl-N-(3-thioxo-3H-1,2,4-dithiazole-5-yl)butanamide (Ia).

DEFINITIONS - Preferred Definitions:
R1 = H or alkyl;
R2 = H, OH, alkyl, alkoxy, H(CxH2xO)m-, aryl, arylalkoxy, arylalkyl, heteroarylalkyl, Het-alkyl or alkylamino;
A = aryl or aryl-Z1-amino aryl, preferably alkoxy phenyl or (alkyl benzoyl) aminophenyl;
R4 = H, arylalkyl or heteroaryl alkyl;
R5-R7 = H, alkyl, alkoxy, H(CxH2xO)m-, alkenyloxy, arylalkoxy, heteroaryl alkoxy, aryl-Z2-amino, alkylamino, aryl, or heteroarylamino;
R10 = H or alkyl; and
Ring B = 1,2,3,4-tetrahydro isoquinoline, pyrrolidine or morpholine.

L81 ANSWER 8 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-291889 [29] WPIX
DNC C2003-076081
TI Preparation for accelerating skin **basement membrane** structure formation, useful for growing artificial skin or for cosmetic skin treatment, comprises a serine protease inhibitor.
DC B04 D21 E11
IN **AMANO, S**; AOYAMA, Y; KOGA, N; **MATSUNAGA, Y**; OGURA, Y; TSUDA, T
PA (SHIS) **SHISEIDO CO LTD**
CYC 34
PI EP 1281396 A2 20030205 (200329)* EN 30 A61K007-48 <--
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
US 2004001897 A1 20040101 (200402) A61K035-78
JP 2004075661 A 20040311 (200419) 33 A61K045-00
CN 1465338 A 20040107 (200423) A61K007-48 <--
KR 2004002424 A 20040107 (200433) A61K007-48 <--
ADT EP 1281396 A2 EP 2002-292849 20021115; US 2004001897 A1 US 2002-314165 20021209; JP 2004075661 A JP 2002-323030 20021106; CN 1465338 A CN 2003-100032 20030106; KR 2004002424 A KR 2003-506 20030106
PRAI JP 2002-323030 20021106; JP 2002-177601 20020618
IC ICM **A61K007-48**; A61K035-78; A61K045-00
ICS **A61K007-42**; A61K031-661; A61K038-00; A61K038-22; A61K038-55; A61K045-06; A61L027-00; A61L027-60; **A61P017-00**; **A61P017-02**; A61P043-00; C12N005-08; C12N009-48
AB EP 1281396 A UPAB: 20030719
NOVELTY - Preparation for accelerating skin **basement membrane** structure formation comprises at least one serine protease inhibitor.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a method for producing artificial skin by culturing an artificial skin-forming medium, comprising adding a serine protease inhibitor to the medium;
(2) a skin external preparation comprising a beech bud extract, a

mint extract and a 1-acyl lysophospholipid of formula (I) or (II).
R1 = a saturated fatty acid residue of 11-24 carbons or a fatty acid residue of 18, 20, 22 or 24 carbons with 1-4 double bonds;
R2 = a saturated fatty acid residue of 13-24 carbons or a fatty acid residue of 18, 20, 22 or 24 carbons with 1-4 double bonds;
M = H or alkali metal.
ACTIVITY - Dermatological.
A human foreskin keratinocyte suspension in KG-DMEM medium was applied to a collagen gel prepared from human dermal fibroblasts. After 4 days, and every 2-3 days thereafter, the medium was replaced with medium containing 10 micro M compound A (a **matrix metalloprotease** inhibitor referred to as N-hydroxy-2-(((4-methoxyphenyl)sulfonyl)-3-picolyl)amino))-3-methylbutaneamide hydrochloride) and 10 micro g/ml aprotinin. The artificial skin formed after 2 weeks was stained with hematoxylin and eosin. Staining of the type VII collagen directly under the basal keratinocytes was greater than when no aprotinin was added.
MECHANISM OF ACTION - Serine protease inhibitor; **Matrix metalloproteinase** inhibitor; Extracellular **matrix** protein production promoter.
USE - The preparation is useful as an additive for culture media for producing artificial skin and (when the serine protease inhibitor is in the form of a mint extract) as a component of a skin treatment composition, especially for reducing roughness and skin aging.
ADVANTAGE - The serine protease inhibitor enhances the accelerating effect of **matrix metalloprotease** inhibitors on **basement membrane** formation.
Dwg.0/9

FS CPI
FA AB; GI; DCN
MC CPI: B04-A08; B04-A09; B04-A10; B04-C01G; B04-H02B; B05-B01P; B14-D07C; **B14-N17**; **D08-B09A1**; E05-G09
TECH UPTX: 20030505
TECHNOLOGY FOCUS - BIOLOGY - Preferred Composition: The serine protease inhibitor is preferably aprotinin, and the preparation also includes a **matrix metalloprotease** inhibitor and a substance that accelerates the production of extracellular **matrix** proteins, especially interleukin-2, transforming growth factor alpha or platelet-derived growth factor.

L81 ANSWER 9 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-759908 [82] WPIX
DNN N2002-598329 DNC C2002-214824
TI Colloidal metal based compositions for detecting skin-aging factors e.g. gelatinase, applicable in developing cosmetics for prevention of skin aging.
DC B04 D16 S03
IN ARAKATSU, H; **INOMATA, S**; KOHNO, Y; NEMORI, R; TAKADA, K
PA (FUJF) FUJI PHOTO FILM CO LTD; (SHIS) **SHISEIDO CO LTD**
CYC 21
PI WO 2002075319 A1 20020926 (200282)* JA 20 G01N033-68
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: US
JP 2002277455 A 20020925 (200282) 7 G01N033-15
ADT WO 2002075319 A1 WO 2002-JP2364 20020313; JP 2002277455 A JP 2001-73427 20010315
PRAI JP 2001-73427 20010315
IC ICM G01N033-15; G01N033-68
ICS C12Q001-37; G01N033-573
AB WO 200275319 A UPAB: 20021220
NOVELTY - Compositions for detecting a skin-aging factor containing microparticles of gold, silver or platinum, are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a method for detecting a skin-aging factor by contacting the composition with a skin tissue; and

(2) a method for judging wrinkle-preventing factor by applying the detection method.

ACTIVITY - Dermatological.

MECHANISM OF ACTION - None given in source material.

USE - The compositions are for detecting skin-aging factor e.g. gelatinase, which are applicable in developing cosmetics for prevention of skin aging.

ADVANTAGE - Such method is simple and easy, with use of cheap reagents for highly-sensitive detection, achieved non-invasively and without influence by bacteria, operable on multi-samples with natural color development as compared to the prior-art methods.

Dwg.0/5

FS CPI EPI

FA AB; DCN

MC CPI: B04-L01; B05-A03B; B11-A02; B11-C08E3; B11-C08F4; B11-C08G; B12-K04E; D05-A02; D05-H09

EPI: S03-E14H

TECH UPTX: 20021220

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Compositions: Such composition is a film-containing a hydrophilic binder.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Compositions: The skin-aging factor can be any of the **MMPs** (matrix metallopropteinases), e.g. gelatinase.

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Detection Methods: The gelatinase is detected in the presence of a horny layer of the skin.

ABEX UPTX: 20021220

EXAMPLE - The composition was prepared with colloidal silver in gelatin applied on a polyester film for fixing on the skin to detect gelatinase (red-black colored when developed).

L81 ANSWER 10 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2002-682787 [73] WPIX

DNC C2002-192646

TI Method of controlling reduction of elasticity of skin accompanied with the reduction of female hormone due to malfunction of ovarium uses **matrix metalloprotease** (sic).

DC B04 D16 D21

IN **INOMATA, S**; OCHIAI, N; TAKADA, K

PA (SHIS) **SHISEIDO CO LTD**; (INOM-I) INOMATA S; (OCHI-I) OCHIAI N; (TAKA-I) TAKADA K

CYC 23

PI WO 2002067873 A2 20020906 (200273)* JA 29 A61K007-00
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: KR US
JP 2002255850 A 20020911 (200275) 10 A61K045-00
EP 1396255 A1 20040310 (200418) EN A61K007-00
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
KR 2003086270 A 20031107 (200418) A61K007-48
US 2004077523 A1 20040422 (200428) A61K031-00

ADT WO 2002067873 A2 WO 2002-JP1757 20020226; JP 2002255850 A JP 2001-50839 20010226; EP 1396255 A1 EP 2002-700812 20020226, WO 2002-JP1757 20020226; KR 2003086270 A KR 2003-711035 20030822; US 2004077523 A1 WO 2002-JP1757 20020226, US 2003-469033 20030826

FDT EP 1396255 A1 Based on WO 2002067873

PRAI JP 2001-50839 20010226

IC ICM A61K007-00; A61K007-48; A61K031-00; A61K045-00
ICS A61K007-40; A61K035-78; A61P005-24; A61P005-30; A61P015-12; A61P017-00

AB WO 200267873 A UPAB: 20021113
NOVELTY - Method of controlling reduction of elasticity of skin accompanied with the reduction of female hormone due to malfunction of ovarium uses **matrix metalloprotease** inhibitor(sic).
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a similar method wherein mangostein (sic) extract is used as the **matrix metalloprotease.**
ACTIVITY - Dermatological.
MECHANISM OF ACTION - None given.
USE - The method is suitable for symptoms of menopause causing sagging of skin.
Dwg.0/2
FS CPI
FA AB; DCN
MC CPI: B14-D01B; B14-D01C; B14-N17; B14-R01; D05-A02C; D08-B09A1; D08-B09A3
TECH UPTX: 20021113
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Inhibitor: Gelatinase (sic) is used as the protease and is coated onto the skin.

L81 ANSWER 11 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-263510 [31] WPIX
DNC C2002-078765
TI Diarylheptanoid derivatives and **matrix metalloprotease** inhibitors from hydrophilic fractions of Curcuma plants (Zingiberaceae) are used in the treatment of e.g. rheumatoid arthritis.
DC B05
PA (SHIS) **SHISEIDO CO LTD**
CYC 1
PI JP 2002030081 A 20020129 (200231)* 18 C07D313-00
ADT JP 2002030081 A JP 2000-212988 20000713
PRAI JP 2000-212988 20000713
IC ICM C07D313-00
ICS A61K007-00; A61K007-035; A61K031-335; A61K035-78; A61P001-02; A61P001-04; A61P017-00; A61P017-02; A61P017-16; A61P019-02; A61P019-10; A61P027-04; A61P029-00; A61P035-00; A61P043-00
AB JP2002030081 A UPAB: 20020516
NOVELTY - New diarylheptanoid derivatives (I) and new **matrix metalloprotease** inhibitory agents from hydrophilic fractions of Curcuma plants, and their new cosmetic compositions and new skin external agents are presented.
DETAILED DESCRIPTION - Diarylheptanoid derivatives of formula (I), hydrophilic hexane-insoluble fractions obtainable from Curcuma plants (Zingiberaceae), their **matrix metalloprotease** inhibitory agents, and cosmetic compositions and skin external agents containing the hexane-insoluble fractions as the effective component are prepared.
R1, R2 = H, 1-6C alkyl or 2-7C acyl; and
carbon-carbon bonds a and b = single or double bonds.
ACTIVITY - Antiarthritic; Antirheumatic; Osteopathic; Cytostatic; Neuroprotective; Ophthalmological; Antiulcer; Cardiovascular active.
Biological data not given in the source material.
MECHANISM OF ACTION - **Matrix metalloprotease** inhibitors.
USE - The diarylheptanoid derivatives are useful in the treatment/prevention of rheumatoid arthritis, osteoarthritis, osteoporosis, ectopic angiogenesis,multiple sclerosis, tumor metastasis or corneal ulcer.
ADVANTAGE - The agents show potent inhibitory activity against **matrix metalloproteases (MMPs)** (e.g., **MMP**-1, -3, and -9).
Dwg.0/0
FS CPI
FA AB; GI; DCN

MC CPI: B06-A02; B14-C09A; B14-C09B; B14-D07C; B14-F02F2; B14-H01B; B14-N01; B14-N03; B14-S01
ABEX UPTX: 20020516
EXAMPLE - Dried rhizomes of Curcuma (5 kg) was soaked two times in ethanol for 7 days at room temperature. The extracts were combined and concentrated to dryness to leave a residue (405 g). This was divided into a hexane-soluble (84 g) and an insoluble (320 g) fractions. The insoluble part (320 g) was subjected to silicon dioxide (SiO2) gel column chromatography in 5% acetone/CHCl3 to MeOH to give an active MeOH-soluble eluate (120 g). This was further chromatographed on SiO2 gel three times in CHCl3/MeOH/H2O (9:1:0.05, 9:1:0.05, and 95:5:0.2) to give an active fraction (2.5 g). This was subjected to Sephadex LH-20 column chromatography in 8:2 MeOH/H2O to give an active fraction. This was further subjected to preparative HPLC two times (ODS, eluent = 8:7 MeCN/H2O and 8:7 MeOH/H2O) to produce 6,11-dihydroxy-3-(4-hydroxy-3-methoxyphenethyl)-7-((E)-4-(4-hydroxy-3-methoxyphenyl)-2-oxo-3-butenyl)-10-methoxy-2-oxabicyclo(6,3,1)dodeca-1(11),8(12),9-trien-5-yl (E)-3-(4-hydroxy-3-methoxyphenyl)-2-propenoate (34 mg).

L81 ANSWER 12 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-108302 [15] WPIX
DNC C2002-033369
TI Elaidyl-lysyl-phenylalanyl-lysine useful as an anti-ageing additive in cosmetic compositions.
DC D21 E14
IN BELLON, G; BELLON, P; BERTON, A; HORNEBECK, W
PA (SHIS) **SHISEIDO INT FRANCE SAS**
CYC 1
PI FR 2810323 A1 20011221 (200215)* 19 C07K005-068
ADT FR 2810323 A1 FR 2000-7726 20000616
PRAI FR 2000-7726 20000616
IC ICM C07K005-068
ICS A61K007-42; A61K007-48
AB FR 2810323 A UPAB: 20020306
NOVELTY - The lipopeptide, elaidyl-lysyl-phenylalanine-lysine(elaidyl-KFK) has been found to activate the peptide TGF beta 1, which is one of the most important regulators in the synthesis of the dermal skin layer.
DETAILED DESCRIPTION - The product elaidyl-lysyl-phenylalanine-lysine of the following formula (I) is new.
INDEPENDENT CLAIMS are also included for:
(1) preparation of (I); and
(2) cosmetic compositions containing the new product.
USE - The new lipopeptide and compositions containing it can be used for the prevention and treatment of ageing marks of the skin, such as wrinkles, produced intrinsically (chrono-induced) or extrinsically (photo-induced).
ADVANTAGE - The additive can easily be incorporated in any cosmetic composition comprising a fatty phase. It is stable in time towards acid or basic pH, O2, water and electrolytes, and is compatible with other common additives such as fatty products, organic solvents, dyes, thickeners, stabilizers, softeners, silicones, perfumes, surfactants, preservatives and any other component used in cosmetics particularly for preparation of emulsions. The lipopeptide has the property of activating the synthesis of the dermal **matrix** by stimulation of the growth factor TGF beta 1 responsible for the anabolism of the macromolecules of the extracellular **matrix** ; at the same time it attenuates degradation reactions of the dermal **matrix** by inhibition of the **metalloproteinases** and protection of the components of the **matrix** against the action of these enzymes.
Dwg.0/2
FS CPI
FA AB; GI; DCN
MC CPI: D08-B09A; E10-B01A1

TECH UPTX: 20020306
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) is prepared by reaction of elaidic acid with lysyl- phenylalanyl-lysine or successively with lysine, phenylalanine and lysine, optionally in their protected forms.
Preferred Composition: The cosmetic composition preferably contains elaidyl-KSK as active agent and an excipient including a fatty phase. The composition comprises a water-in-oil or oil-in-water emulsion, and is in the form of a cream. The composition also contains organic or inorganic solar filters, UVB and UVA. The compositions may also contain other anti-ageing agents such as anti-radical agents(tocopherols, vitamins E and C, carotenoids, etc.), anti-glycation compounds or alpha or beta-hydroxyacids.
ABEX UPTX: 20020306
EXAMPLE - An example of the preparation of an anti-wrinkle daytime cream composition was as follows :Phase A : Octyl hydroxystearate: 5 g ; Propylene glycol-15 stearyl ether: 6 g ; Glyceryl stearate: 2 g ; MYRJ 49 (RTM: emulsifier): 1.8 g ; Lipopeptide elaidyl-KFK : 1 g ; Cis-parinarique acid: 1 g; Parabens : qs ; Phase B : Water : qs ; Glycerine: 3 g ; Butylene glycol: 2 g ; Additives (butylhydroxytoluene, dyes, EDTA): qs ; Phase C : SEPIGEL 305 (RTM: gelling agent); Phase D: Perfume : qs ; (qs = sufficient quantity). The phases A and B were heated to 80 degreesC. Phase A was then incorporated with phase B, then cooled to 45 degreesC. with stirring. Phase C was added and then phase D.

L81 ANSWER 13 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-089877 [12] WPIX
DNC C2002-027724
TI External skin preparations for suppressing sebum secretion comprise **metalloproteinase** inhibitor.
DC B03 D21
IN **INOMATA, S**; KOBAYASHI, K
PA (SHIS) **SHISEIDO CO LTD**; (INOM-I) INOMATA S; (KOBA-I) KOBAYASHI K
CYC 24
PI WO 2001089471 A2 20011129 (200212)* JA 26 A61K007-48
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: CN KR US
JP 2002047125 A 20020212 (200227) 14 A61K007-00
EP 1284134 A2 20030219 (200321) EN A61K007-48
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
KR 2003005381 A 20030117 (200334) A61K007-48
CN 1427714 A 20030702 (200361) A61K007-48
US 2004009241 A1 20040115 (200406) A61K035-78
ADT WO 2001089471 A2 WO 2001-JP4336 20010523; JP 2002047125 A JP 2001-151391 20010521; EP 1284134 A2 EP 2001-932233 20010523, WO 2001-JP4336 20010523; KR 2003005381 A KR 2002-715767 20021122; CN 1427714 A CN 2001-809227 20010523; US 2004009241 A1 WO 2001-JP4336 20010523, US 2002-277000 20021120
FDT EP 1284134 A2 Based on WO 2001089471
PRAI JP 2001-151391 20010521; JP 2000-197309 20000526
IC ICM A61K007-00; A61K007-48; A61K035-78
ICS A61K031-12; A61K031-19; A61K031-4406; A61K045-00; A61P017-00
AB WO 200189471 A UPAB: 20020221
NOVELTY - External skin preparations for suppressing sebum secretion comprise a **metalloproteinase** inhibitor.
ACTIVITY - Endocrine-Gen; Dermatological.
In tests using the hairless mouse model 10 micro l of a composition comprising 1% N-hydroxy-2(R)-((4-methoxyphenyl)sulfonyl)(3-picolyl)amino)-3-methylbutanamide (I) applied 3 times a day for a week reduced sebum secretion by 79%.
MECHANISM OF ACTION - **Matrix-Metalloproteinase** -Inhibitor.
USE - As external skin preparations for suppressing sebum secretion

useful for treating and preventing spots and hair loss.
Dwg.0/4
FS CPI
FA AB; DCN
MC CPI: B04-A08C2; B04-A10; B07-D04C; B14-D07C; B14-N17; B14-R02; D08-B03; D08-B09A1
TECH UPTX: 20020221
TECHNOLOGY FOCUS - PHARMACEUTICALS - More Specifically:
Metalloproteinase inhibitor is N-hydroxy-2(R)-((4-methoxyphenyl)sulfonyl)(3-picolyl))-3-methylbutanamide of formula (I) or its hydrochloride salt or is an extract of Potenilla formentilla S., Persa americana Mill., Garcinia mangostana L, Cocos nucifera L, Blumea balsamifera (L) DC. or Cinnamomum cassia Bl..
ABEX UPTX: 20020221
ADMINISTRATION - Administration is topically using a composition comprising 0.0001-20 weight% active agent.

L81 ANSWER 14 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-605339 [69] WPIX
DNC C2001-179636
TI **Matrix metallo protease** inhibitor for preventing aging of skin, and for use in skin external preparation, comprises plant extract such as Symplocos racemosa, Cyperus rotundus, Acacia fornensia and/or Cassia fistula.
DC B04 D21
PA (SHIS) **SHISEIDO CO LTD**
CYC 1
PI JP 2001192317 A 20010717 (200169)* 9 A61K007-00 <--
ADT JP 2001192317 A JP 2000-5705 20000106
PRAI JP 2000-5705 20000106
IC ICM **A61K007-00**
ICS **A61K007-021**; **A61K007-40**; A61K035-78; **A61P017-16**; A61P043-00
AB JP2001192317 A UPAB: 20011126
NOVELTY - A **matrix metallo protease** (**MMPs**) inhibitor belonging to gelatinase group, is also an inhibitor of elastin degradation, laminin degradation and **basement membrane** degradation, or **MMPs** inhibitor belonging to stromelysin group is also an inhibitor of proteoglycan degradation. The inhibitor comprises plant extract such as Symplocos racemosa, Cyperus rotundus and/or Acacia fornensia.
DETAILED DESCRIPTION - **MMPs** inhibitor belonging to gelatinase group is also an inhibitor of elastin degradation, laminin degradation, **basement membrane** degradation, or **MMPs** inhibitor belonging to stromelysin group is also an inhibitor of proteoglycan degradation. The inhibitor comprises plant extract such as Symplocos racemosa, Cyperus rotundus, Acacia fornensia, Cyperus scariosus, Gaultheria fragrantissima, Terminalia chebula, Ficus bengalensis, Cassia fistula, Lyonia ovalifolia, Calophyllum inophyllum and/or Ficus religiosa.
ACTIVITY - None given in source material.
MECHANISM OF ACTION - Inhibitors of **matrix metallo protease** (**MMPs**); elastin degradation; laminin degradation; **basement membrane** degradation; proteoglycan degradation. **MMPs** inhibitory effect was evaluated by adding **MMP9** enzyme isolated from human cell, to type IV collagen, in presence of Acacia fornensia test sample. The test sample is obtained by dissolving ethanol extract of Acacia fornensia in dimethylsulfoxide to obtain 2 weight% solution which was diluted to predetermined concentration. The inhibitory rate of **MMP9** was measured, by comparing the substrate decomposition ratio in the group containing the test sample and the group containing ethylene diamine tetra acetic acid (EDTA) (reference sample). The results obtained showed that the test sample at 0.0005% of concentration showed 95% of inhibitory

effect, when compared with EDTA which at 0.05% of concentration showed 90% of inhibitory effect. Thus, the plant extract showed excellent **MMPs** inhibitory effect.

USE - For preventing aging, slack and wrinkles of skin, and for use in make-up cosmetics, hair cosmetics, bath liquid, and skin external preparation such as ointment, cream, milky lotion, lotion pack, jelly, essence, pack, solid foundation, emulsifying-type foundation and bath agent.

ADVANTAGE - The **matrix metallo protease** (**MMPs**) inhibitor has excellent **MMP9** activated inhibitory effect and **MMP3** activated inhibitory effect. The inhibitor efficiently prevents degradation of skin extra-cellular **matrix** component by **MMPs**. The inhibitor effectively maintains the skin without any wrinkles and slack, and prevents aging of skin. Hence, youthful skin is effectively maintained.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B04-A10; **B14-N17**; **B14-R01**; **D08-B09A**
ABEX UPTX: 20011126

EXAMPLE - (In weight%) Carboxy vinyl polymer (Carbo pole 941) (0.05) was dissolved in small amount of ion exchange water (quantity sufficient (q.s)), to obtain phase-A. Polyethylene glycol 1500 (3.0) and triethanolamine (1.0), were added to the remaining ion exchange water, heat-dissolved, and maintained at 70degreesC, to obtain a water phase. Stearic acid (2.5), cetyl alcohol (1.5), vaseline (5.0), liquid paraffin (10.0), polyoxyethylene (10 mols), mono oleate (2.0), Acacia fornensia extract (ethyl acetate ester extract) (0.01), sodium hydrogen sulfite (0.01), ethyl paraben (0.3) and fragrance (q.s), were mixed, heat-fused, and maintained at 70degreesC, to obtain an oil phase. The oil phase was added to the water phase, pre-emulsified. Then, phase-A was added, uniformly emulsified, and cooled to 30degreesC with agitation, to obtain a milky lotion.

L81 ANSWER 15 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-602815 [68] WPIX
DNN N2001-449794 DNC C2001-178628
TI Agents e.g. for promoting formation of skin **basement membrane** comprise **matrix metalloprotease** inhibitor.
DC B03 D21 P34
IN **AMANO, S**; INOMATA, S; **MATSUNAGA, Y**; **INOMATA, S**
PA (SHIS) **SHISEIDO CO LTD**; (AMAN-I) AMANO S; (INOM-I) INOMATA S; (MATS-I) MATSUNAGA Y
CYC 24
PI WO 2001072347 A1 20011004 (200168)* JA 35 A61L027-60
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: CN KR US
JP 2001269398 A 20011002 (200172) 17 A61L027-00
EP 1180371 A1 20020220 (200221) EN A61L027-60
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
KR 2002019920 A 20020313 (200263) A61L027-60
CN 1365293 A 20020821 (200281) A61L027-60
US 2002193875 A1 20021219 (200303) A61F002-14
US 2004038859 A1 20040226 (200416) A61K031-00
ADT WO 2001072347 A1 **WO 2001-JP2507 20010327**; JP 2001269398 A **JP 2000-87574 20000327**; EP 1180371 A1 EP 2001-915860 20010327, **WO 2001-JP2507 20010327**; KR 2002019920 A KR 2001-714980 20011123; CN 1365293 A CN 2001-800673 20010327; US 2002193875 A1 **WO 2001-JP2507 20010327, US 2001-979712 20011126**; US 2004038859 A1 **Cont of WO 2001-JP2507 20010327, Cont of US 2001-979712 20011126**, US 2003-648485 20030827
FDT EP 1180371 A1 Based on WO 2001072347

PRAI **JP 2000-87574 20000327**
IC ICM A61F002-14; A61K031-00; A61L027-00; A61L027-60
ICS **A61K007-00**; **A61K007-40**; **A61K007-48**;
A61K031-44; A61K035-78; A61K038-07; A61K045-00; A61K045-06;
A61K047-00; A61L027-54; **A61P017-00**
AB WO 200172347 A UPAB: 20011121
NOVELTY - Agents for promoting the formation of skin **basement membrane** or for promoting the formation of artificial skin comprise a **matrix metalloprotease** inhibitor.
ACTIVITY - Dermatological.
In an artificial skin production model using human dermal cells addition of CGS27023A (10 micro M) increased formation of artificial skin (no specific results given).
MECHANISM OF ACTION - **Matrix-Metalloproteinase** -Inhibitor.
USE - For promoting the formation of skin **basement membrane** or for promoting the formation of artificial skin.
Dwg.0/4
FS CPI GMPI
FA AB; DCN
MC CPI: B04-A10; B04-N04A; B14-D07C; **B14-N17**; **B14-R01**; **D08-B09A**
TECH UPTX: 20011121
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Agent: The agent also comprises a matrix protein production promoter. The agent is e.g. a plant extract (e.g. Paconiaceae, Thcaccae or Rubiaceae) or p-NH2-Bz-Gly-Pro-DLeu-Ala-NHOH.
ABEX UPTX: 20011121
ADMINISTRATION - Administration is topically in a composition containing 0.000001-60 (preferably 0.00001-60) weight.% active agent.

L81 ANSWER 16 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-631183 [61] WPIX
DNC C2000-189748
TI Antiageing agent as make-up cosmetics, cosmetics for hair or as bath liquid, comprises active ingredient obtained from specific genus.
DC B04 D21
PA (SHIS) **SHISEIDO CO LTD**
CYC 1
PI JP 2000226311 A 20000815 (200061)* 9 A61K007-00
ADT JP 2000226311 A JP 1999-26775 19990203
PRAI JP 1999-26775 19990203
IC ICM A61K007-00
ICS A61K007-48; A61K035-78; A61P017-00; A61P043-00
AB JP2000226311 A UPAB: 20001128
NOVELTY - An antiageing agent (I) comprises an active ingredient obtained from Potentilla of Rosaceae.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) for cosmetics containing (I); and (2) a collagenase activity inhibitor containing (I).
ACTIVITY - Endocrine-gen. No test details are given in the specification.
MECHANISM OF ACTION - Antagonizes collagenase activity, especially **MMP1** (**matrix metalloprotease**) activity. An extract of Tormentilla was prepared by immersing the root in ethanol for 1 week at room temperature. The extract was added with buffer solution and the collagenase activity inhibitory effect was determined. A fluorescein isothionate was labeled as substrate to a collagenase enzyme. The enzyme was mixed with the extracted sample solution and incubated at 37 deg. C for 2-4 hours. Ethanol was added to the solution for settling the unreacted collagen. The fluorescein intensity of degraded collagen present in the supernatant liquid was measured for determining the decomposition ratio. A comparative test was performed by utilizing EDTA (Ethylene

Diamine Tetra Acetic acid). The result showed the ratio of collagen activity inhibitory effect of the extract was found to be extremely superior to that of EDTA.

USE - As make-up cosmetics, cosmetics for hair and as a bath liquid.

ADVANTAGE - The formulation inhibits collagenase activity excellently, thereby preventing the degradation of collagen. The ageing of skin is prevented and an improved youthful skin is maintained.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B04-A08; B04-A10; B14-N17; B14-R01; D08-B03; D08-B09A
TECH UPTX: 20001128

TECHNOLOGY FOCUS - BIOLOGY - Preferred Plant: The genus of Potentilla is Tormentilla.

ABEX UPTX: 20001128

ADMINISTRATION - Administered externally.

EXAMPLE - (In weight%) Propylene glycol (10), Tormentilla extract 0.01 and caustic potash (0.2) were added and dissolved in ion exchange water at 70degreesC to obtain a water phase. A mixture containing stearic acid (5), stearyl alcohol (4), isopropyl myristate (18) and glyceryl monostearate (3) was added and heat fused with sodium hydrogen sulfite (0.01), preservative (required amount) and flavoring agent at 70degreesC to obtain a oil phase. The oil phase was gradually added to the water phase and emulsified uniformly in a homo mixture at 30degreesC with constant stirring to obtain a cream. A hundred healthy females of age group 25-60 years were made to apply the cosmetics everyday for 1 month. The improvement of wrinkles were visually observed. The cosmetics were found to have an excellent antiageing effect.

L81 ANSWER 17 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-579204 [54] WPIX
DNC C2000-172392
TI Dermatological preparation for preventing skin aging comprises substance obtained by extracting a crude drug.
DC B04 D21
IN **INOMATA, S**; OKAZAKI, T; OTA, M; SUZUKI, Y; UMISHIO, K
PA (SHIS) **SHISEIDO CO LTD**
CYC 8
PI WO 2000051562 A1 20000908 (200054)* JA 47 A61K007-48
RW: DE FR GB IT
W: CN KR US
JP 2000256122 A 20000919 (200060) 8 A61K007-00
JP 2001139466 A 20010522 (200134) 11 A61K031-121
JP 2001192316 A 20010717 (200144) 11 A61K007-00
ADT WO 2000051562 A1 WO 2000-JP1260 20000303; JP 2000256122 A JP 1999-54949 19990303; JP 2001139466 A JP 1999-320747 19991111; JP 2001192316 A JP 2000-5704 20000106
PRAI JP 2000-5704 20000106; JP 1999-54949 19990303; JP 1999-320747 19991111
IC ICM A61K007-00; A61K007-48; A61K031-121
ICS A61K007-02; A61K007-031; A61K007-06; A61K007-50; A61K035-78; A61P017-00; A61P017-16; A61P043-00
AB WO 200051562 A UPAB: 20001027

NOVELTY - Dermatological preparation for preventing skin aging comprising a substance obtained by extracting a crude drug or its component with human skin **matrix metalloprotease** (**MMP**) inhibitory activity, is new.

ACTIVITY - Dermatological.

MECHANISM OF ACTION - Collagenase-inhibitor; Stromelysin-Inhibitor; Gelatinase-Inhibitor-B.

In assays an ethanolic extract from Thymus serpyllum) at 0.05 wt% inhibited 100% of **MMP**-1 and **MMP**-9 activity and

inhibited 85% of **MMP**-3 activity. The correspoding values for ethylenediamine tetraacetate at 0.05 wt% were 89, 90 and 82 % respectively.

USE - As a dermalogical preparation useful e.g. as cosmetics for preventing skin aging.

ADVANTAGE - Preparation contains natural products with at least the same activity as ethylenediamine tetraacetate.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B04-A08C2; B04-A10; B04-M01; B12-M02; B14-D07C; B14-N17; B14-N17C; D08-B09A

TECH UPTX: 20001027

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Agent: The active agent (at 0.001-0.0005 wt%) has at least equivalent activity to ethylenediamine tetraacetate against **MMP** (preferably **MMP**-9, **MMP**-3 and/or **MMP**-1) and is obtained by extracting a plant of the genus Labiatae (e.g. Thymus serpyllum), Rosaceae, Tiliaceae, Leguminosae, Theaceae, Guttiferae, Valerianaceae, Ebenaceal, Ranunculaceae, Myrtaceae, Betulaceae, Rubiaceae and/or Juglandaceae (e.g. Sophora flavescens Aiton), or Curcuma and/or Zingiberaceae.

ABEX UPTX: 20001027

EXAMPLE - A cream for preventing skin aging comprised (by wt%) stearic acid (5.0), stearyl alcohol (4.0), isopropyl myristate (18.0), glyceryl monostearate (3.0), propylene glycol (10.0), curcumine (0.001), potassium hydroxide (0.2), sodium bisulphite (0.01) and perservatives, fragrance and deionised water (to 100%).

L81 ANSWER 18 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2000-208858 [19] WPIX

DNC C2000-064543

TI Use of fatty acids, especially elaidic acid, trans-parinaric acid and cis-parinaric acid are **matrix metalloproteinase** inhibitors for cosmetic treatment of signs of aging.

DC B05 D21 E13 E17

IN BELLON, G; BELLON, P; BERTON, A; HORNEBECK, W

PA (SHIS) **SHISEIDO INT FRANCE SA**; (SHIS) **SHISEIDO INT FRANCE SAS**

CYC 27

PI FR 2782638 A1 20000303 (200019)* 24 A61K007-48
EP 985409 A1 20000315 (200019) FR
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2000072653 A 20000307 (200023) 11 A61K007-48
KR 2000017609 A 20000325 (200104) A61K007-48

ADT FR 2782638 A1 FR 1998-10823 19980828; EP 985409 A1 EP 1999-402088 19990819; JP 2000072653 A JP 1999-239622 19990826; KR 2000017609 A KR 1999-36037 19990828

PRAI FR 1998-10823 19980828

IC ICM A61K007-48
ICS A61K007-00

AB FR 2782638 A UPAB: 20011203

NOVELTY - The fatty acids (I) are used in cosmetics for preventing and/or treating the signs of aging.

DETAILED DESCRIPTION - The fatty acids of formula (I) or their salts are used in cosmetics. R3-R-CHR1-CHR2-(CH2)5-COOH (I)

R1 and R2 = H or OH;

R = -CH=CR4-, -CC-, epoxy or monohydroxy epoxy;

R3 = 6-12C aliphatic group with 1 - 4 unsaturations which may be ethylenic or acetylenic; and

provided that the carbon atom in position 12 may be substituted by OH, and the carbon atoms in positions 11 and 12, and/or 12 and 13 may form epoxy groups.

ACTIVITY - Dermatological. The hydrolysis of a substrate by **MMP**-1, **MMP**-2, and **MMP**-3 was measured in the presence and absence of elaidic acid, and the inhibition constant (Ki) calculated with the following results: **MMP**-1: 2.7 mu M; **MMP**-2: 4.25 mu M; **MMP**-3: 1.8 mu M.

MECHANISM OF ACTION - **Matrix metalloproteinase** (especially **MMP**-1, **MMP**-2, **MMP**-9 and leucocytary elastase) inhibitors (claimed).

USE - (I) are useful in cosmetic treatment for preventing and/or treating the signs of aging, whether chrono-induced or photo-induced, and for inhibiting the enzymatic activity of **matrix metalloproteinases** and so protecting the skin against their effects.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B04-C03; B10-C02; B10-C04E; B10-E04C; B14-R01; D08-B09A
TECH UPTX: 20011203

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: Cosmetic compositions contain (I) 0.01-20 wt. % and also other known active ingredients, excipients and diluents.

ABEX UPTX: 20011203

SPECIFIC COMPOUNDS - The use of elaidic acid, trans-parinaric acid, and cis-parinaric acid is specifically claimed.

ADMINISTRATION - Administration is topical (claimed).

EXAMPLE - An anti-wrinkle cream contained (g): octyl hydroxystearate (5), polypropylene glycol-15 stearyl ether (5), glyceryl stearate (2), MYRJ 49 (RTM) (emulsifier, 1.8), trans-parinaric acid (2), elaidic acid (1), cis-parinaric acid (1), parabens as required. Separately glycerin (3 g) and butylene glycol (2 g) were mixed in water with anti-oxidants, preservatives, colors and EDTA. These two mixtures were both heated to 80 degreesC and the oily phase added to the aqueous phase. The mixture was cooled to 45 degreesC and an emulsifier Sepigel 305 (RTM: gelling agent) (2 g) and a perfume were added, the mixture being stirred vigorously to give an oil-in-water emulsion.

DEFINITIONS - Preferred Definition:
R = -CH=CH- (in trans conformation).

L81 ANSWER 19 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-085515 [07] WPIX
CR 2000-610771 [58]
DNC C2000-023833
TI Composition useful for preventing and treating conditions associated with connective tissue or **basement membrane** degradation.
DC B05
IN GOLUB, L M; RAMAMURTHY, N S; SALO, T A; SORSA, T A; TERONEN, O P
PA (UYNY) UNIV NEW YORK STATE RES FOUND
CYC 90
PI US 5998390 A 19991207 (200007)* 17 A01N052-00
WO 2000018230 A1 20000406 (200025) EN A01N037-18
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 9961620 A 20000417 (200035) A01N037-18
EP 1117296 A1 20010725 (200143) EN A01N037-18
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

KR 2001075220 A 20010809 (200211) A61K031-662
JP 2002525294 W 20020813 (200267) 37 A61K031-663
AU 755871 B 20030102 (200319) A01N037-18

ADT US 5998390 A US 1998-161804 19980928; WO 2000018230 A1 WO 1999-US22199 19990924; AU 9961620 A AU 1999-61620 19990924; EP 1117296 A1 EP 1999-948446 19990924, WO 1999-US22199 19990924; KR 2001075220 A KR 2001-703547 20010320; JP 2002525294 W WO 1999-US22199 19990924, JP 2000-571758 19990924; AU 755871 B AU 1999-61620 19990924

FDT AU 9961620 A Based on WO 2000018230; EP 1117296 A1 Based on WO 2000018230; JP 2002525294 W Based on WO 2000018230; AU 755871 B Previous Publ. AU 9961620, Based on WO 2000018230

PRAI US 1998-161804 19980928

IC ICM A01N037-18; A01N052-00; A61K031-662; A61K031-663
ICS A01N057-00; A61K031-65; A61K031-66; A61P001-02; A61P001-04; A61P009-00; A61P011-00; A61P011-06; **A61P017-02**; **A61P017-06**; A61P019-00; A61P019-02; A61P019-10; A61P027-02; A61P029-00; A61P031-18; A61P035-00; C12N009-64; C12N009-99

AB US 5998390 A UPAB: 20030320

NOVELTY - Inhibiting the production and activity of proteinases in a biological system by administering a composition (I) comprising a synergistic combination of tetracycline and bisphosphonate, is new.

ACTIVITY - Osteopathic; cytostatic; antiarthritic.

MECHANISM OF ACTION - Bone-resorption suppressant.

Recombinant human **matrix metalloproteinase** (**MMP**-14) was pretreated with buffer and combinations of 2 mu M 6-dimethyl-6-deoxy-4-de(dimethylamino) tetracycline (CMT-3) and 2 mu M bisphosphonate clodronate for 1 hour at 37 deg. C. Substrate beta -casein (52 mu M) was added and incubated for 1 hour at 37 deg. C. Incubation was terminated by adding Laemli's sample buffer and boiled for 5 minutes before SDS-PAGE and quantitative laser-densitometric analysis. The results indicated that the combination of CMT-3 and bisphosphonate clodronate synergistically inhibited beta -casein degradation by pure recombinant human **MMP**-14.

USE - The method is useful for inhibiting excess production and activity of proteinases in mammals associated with connective tissue and/or **basement membrane** degradation. Tissue degradation includes tissue invasion and metastasis by malignant cells, osteoporotic bone loss, bone resorption cartilage destruction, angiogenesis or destruction of soft tissue (claimed).

(I) can used in the form of a cosmetic preparation. The method is also useful for preventing and/or treating mammalian diseases such as periodontitis, osteoarthritis, rheumatoid arthritis, cancer, osteomyelitis, osteoporosis, osteosarcoma and other bone diseases.

ADVANTAGE - (I) does not have any adverse side-effects.

Dwg.0/8

FS CPI

FA AB; DCN

MC CPI: B02-T; B05-B01F; B05-B01G; B05-B01N; B05-B01P; B14-C09A; B14-C09B; B14-D07C; B14-H01; B14-N01; B14-N06B; B14-S09

TECH UPTX: 20000209

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Compounds: The tetracycline is preferably CMT-1,CMT-3,CMT-8,doxycycline, minocycline, lymecycline and bisphosphonate, preferably alendronate, clodronate, etidronate, pamidronate, medronate, nedrinate, tiludronate, zolendronate or combinations is present in synergistic amounts for inhibiting the production and activity of excess proteinase. (I) further comprises a pharmaceutical preparation or carrier and inhibits the activity of proteinases preferably **matrix metalloproteinase** (**MMP**), an **MMP**-like enzyme or a serine proteinase or their combinations.

ABEX UPTX: 20000209

ADMINISTRATION - Administration can be oral, parenteral, topical or subcutaneous. Dosage is 10-1000 mg/day of tetracycline in combination

with 20-2000 mg/day of bisphosphonate.

L81 ANSWER 20 OF 20 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1990-290097 [38] WPIX
CR 1998-051544 [05]
DNC C1990-125215
TI New **matrix metallo-proteinase** inhibitor - used to treat diseases resulting from **matrix metallo-proteinase** activity and in diagnosis, detection and purificn..
DC B04 D16
IN KRUTZSH, H; LIOTTA, L A; STETLER-STEVENSON, W G; KRUTZSCH, H C; STETLERSTE, W G; KRUTZSCH, H
PA (USDC) US DEPT OF COMMERCE; (USSH) NAT INST OF HEALTH; (USDC) US SEC OF COMMERCE; (USSH) US DEPT HEALTH & HUMAN SERVICES
CYC 16
PI US 494796 A0 19900821 (199038)* 54
WO 9011287 A 19901004 (199042)
AU 9053591 A 19901022 (199104)
EP 464147 A 19920108 (199202) 54
JP 04504418 W 19920806 (199238) C07K007-10
AU 634533 B 19930225 (199315) C12N015-15
EP 464147 A4 19920819 (199523)
US 5595885 A 19970121 (199710) 23 C12N015-00
JP 3156082 B2 20010416 (200124) 23 C07K014-435
EP 464147 B1 20020626 (200242) EN C07K014-81
R: AT BE CH DE DK ES FR GB IT LI LU NL SE
DE 69033982 E 20020801 (200258) C07K014-81
ADT US 494796 A0 US 1990-494796 19900313; EP 464147 A EP 1990-905905 19900321; JP 04504418 W JP 1990-505523 19900321, WO 1990-US1526 19900321; AU 634533 B AU 1990-53591 19900321; EP 464147 A4 EP 1990-905905 ; US 5595885 A CIP of US 1989-326334 19890321, CIP of US 1989-380431 19890717, CIP of US 1989-395453 19890818, Cont of US 1990-494796 19900313, US 1993-39525 19930329; JP 3156082 B2 JP 1990-505523 19900321, WO 1990-US1526 19900321; EP 464147 B1 EP 1990-905905 19900321, WO 1990-US1526 19900321; DE 69033982 E DE 1990-633982 19900321, EP 1990-905905 19900321, WO 1990-US1526 19900321
FDT JP 04504418 W Based on WO 9011287; AU 634533 B Previous Publ. AU 9053591, Based on WO 9011287; JP 3156082 B2 Previous Publ. JP 04504418, Based on WO 9011287; EP 464147 B1 Based on WO 9011287; DE 69033982 E Based on EP 464147, Based on WO 9011287
PRAI US 1990-494796 19900313; US 1989-326334 19890321;
US 1989-380431 19890717; US 1989-395453 19890818;
US 1993-39525 19930329
REP 3.Jnl.Ref; EP 404750
IC ICM C07K007-10; C07K014-435; C07K014-81; C12N015-00; C12N015-15
ICS A01N037-18; A61K035-12; A61K037-02; A61K037-64; A61K038-57; A61K039-00; A61K048-00; C07H015-12; C07K007-08; C07K013-00; C12N000-01; C12N001-21; C12N001-22; C12N015-09; C12P021-02; C12P021-08; G01N033-53; G01N033-573
AB US N7494796 N UPAB: 20020910
A novel inhibitor of metalliproteinases designated TIMP-2 is disclosed. Also disclosed is DNA encoding TIMP-2.
USE - The TIMP-2 inhibits **matrix metalloproteinases** and can be used for treating diseases such as arthritis, diabetes, cancer, ulcers of mucosa and epithelial tissues, antoimmune mediated inflammation, lung injury, granulomatous diseases and myecardial infarctions. Other therapeutic benefit may also be obtd. in diseases with **basement membrane** destruction such as lupus, autoimmune neural disorders, myocyte destruction such as myodystrophies, myocardial infarct and glomerulopathies. It can also be used as a birth control agent by preventing embryo/placental attachment or invasion. The TIMP-2 can also be used to produce antibodies. The protein and antibodies can be used in detection, diagnosis and pruifications. The DNA can be used to produce the

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     TIMP-2, in disease diagnosis and prediction and in gene therapy.
     Dwg.0/12
FS   CPI
FA   AB
MC   CPI: B04-B04A1; B04-B04F; B11-C07A; B12-A07; B12-D02A; B12-D03;
          B12-D07; B12-E01; B12-E08; B12-F01B; B12-G01B3; B12-G03; B12-G07;
          B12-H05; B12-J01; B12-K03; B12-K04A; B12-K06; D05-H09; D05-H12
ABEQ US   5595885 A UPAB: 19970307
     An isolated nucleic acid having a sequence which encodes human TIMP-2,
     with the 194 amino acid polypeptide sequence given in the specification,
     is new.
     Dwg.0/12


=> d his

     (FILE 'HOME' ENTERED AT 17:52:36 ON 23 JUN 2004)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 17:55:43 ON 23 JUN 2004
L1           570 S MATRIX(L)?METALLO?/CNS
L2           476 S ?METALLOPROTEASE?/CNS
L3          1457 S ?METALLOPROTEINASE?/CNS
L4          1940 S L1-L3

     FILE 'HCAPLUS' ENTERED AT 17:56:34 ON 23 JUN 2004
L5         15488 S MMP? OR MATRIXMETALLOPROTEASE OR MATRIXMETALLOPROTEINASE OR M
L6         32260 S L4
L7         19379 S ?METALLOPROTEASE? OR ?METALLOPROTEINASE?
L8         37648 S L5-L7
L9          1281 S L8 AND BASEMENT(L)MEMBRANE
L10          185 S L9 AND (SKIN OR EPIDERM? OR DERM?)
                 E BASEMENT MEMBRANE/CT
L11         5139 S E3-E6
L12         5139 S E3+OLD,NT,PFT
                 E E3+ALL
                 E E7+ALL
L13        16556 S E3+NT
L14          647 S L8 AND L11-L13
L15         1465 S L9,L14
                 E SKIN/CT
L16        97199 S E3+OLD,NT,PFT
                 E E3+ALL
L17        97192 S E7,E6+NT
L18          850 S E32+OLD,NT,PFT
L19        10495 S E34+OLD,NT,PFT
L20         6432 S E35+OLD,NT,PFT
L21        68544 S E38+OLD,NT,PFT
                 E SKIN DISEASE/CT
                 E E4+ALL
                 E E2+ALL
L22        68543 S E6,E7,E5+NT
L23          678 S E179+OLD,NT,PFT
                 E E181+ALL
L24         8037 S E3+NT
L25         2906 S E17+OLD,NT,PFT
                 E E17+ALL
L26         4203 S E7+OLD,NT,PFT
L27         8526 S E8+OLD,NT,PFT
                 E E6+ALL
L28         8037 S E3+NT
                 E E14+ALL
L29        65858 S E2,E3,E1+NT
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L30          183 S L15 AND L16-L29
L31          262 S L10,L30
                 E WO2001-JP2507/AP,PRN
L32            1 S E3,E4
                 E US2001-979712/AP,PRN
L33            1 S E3,E4
                 E JP200-87574/AP,PRN
                 E JP2000-87574/AP,PRN
L34            1 S E3,E4
L35            1 S L31 AND L32-L34
L36          194 S L31 AND (PD<=20010327 OR PRD<=20010327 OR AD<=20010327)
                 E AMANO S/AU
L37          137 S E3,E18
                 E MATSUNAGA Y/AU
L38           95 S E3
                 E MATSUNAGA YUK/AU
L39            5 S E6
                 E MATSUNAGA YU/AU
                 E INOMATA S/AU
L40          101 S E3,E22
                 E SHISEIDO/PA,CS
L41         5171 S E3,E4
L42           10 S L31 AND L37-L41
L43            1 S L35 AND L42
L44            1 S L35,L43
L45            9 S L42 NOT L44
L46           39 S L6 (L) INHIBIT? AND L36
                 SEL DN AN 1 6 11 15 16 17 18 19 20 35 37
L47           11 S L46 AND E1-E33
                 SEL DN AN 4 11
L48            9 S L47 NOT E34-E39
L49            9 S L44,L48
L50            5 S L49 NOT BASEMENT
L51          163 S L36 AND BASEMENT
L52            2 S L51 AND ARTIFICIAL(L)SKIN
L53            4 S L36 AND ARTIFICIAL(L)SKIN
L54            8 S L36 AND ARTIFICIAL?
L55            4 S L49 NOT L50
L56           11 S L52-L55
                 SEL DN AN 5 6
L57            9 S L56 NOT E40-E45
L58            4 S L49 NOT L57
L59           22 S L57,L58,L45 AND L5-L58
                 SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 18:19:06 ON 23 JUN 2004
L60           16 S E46-E61
L61           16 S L60 AND L4

     FILE 'REGISTRY' ENTERED AT 18:19:43 ON 23 JUN 2004

     FILE 'HCAPLUS' ENTERED AT 18:19:55 ON 23 JUN 2004

     FILE 'WPIX' ENTERED AT 18:20:25 ON 23 JUN 2004
L62            1 S L32-L34
L63         2501 S L5/BIX OR L7/BIX
L64           32 S L63 AND BASEMENT(L)MEMBRANE/BIX
L65           33 S L63 AND BASEMENT/BIX
L66           33 S L64,L65
L67            8 S L66 AND A61P017/IC,ICM,ICS
L68            6 S L66 AND A61K007-48/IC,ICM,ICS
L69           18 S L66 AND (B14-N17? OR C14-N17? OR B14-R01 OR C14-R01 OR B12-A0
L70           14 S L66 AND (P943 OR Q254)/M0,M1,M2,M3,M4,M5,M6
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L71          19 S L67-L70
L72           8 S L66 AND A61K007/IC,ICM,ICS
L73          19 S L71,L72
                SEL DN AN 1 8 11 12 14-18
L74          10 S L73 NOT E62-E81
L75          10 S L62,L74
L76          19 S L63 AND SHISEIDO?/PA
L77          10 S L63 AND (AMANO S? OR MATSUNAGA Y? OR INOMATA S?)/AU
L78           7 S L76,L77 AND L75
L79          13 S L76,L77 NOT L78
                SEL DN AN 3 9 13
L80          10 S L79 NOT E82-E88
L81          20 S L75,L78,L80 AND L62-L80

     FILE 'WPIX' ENTERED AT 18:32:06 ON 23 JUN 2004

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